been the focus of a PSA campaign in 2008. ED has written a "Short Guide to the EU Guidelines" and translated it into 8 different languages to provide a key tool for advocates to promote these concepts on a national level. This effort has been supported by the European Commission. In addition ED continues to be active at the European Parliament to press for countries to implement these services. While there are 2 resolutions on breast cancer already in existence, it is essential to keep Guideline implementation on the public health agenda. ED provided input into the Declaration on breast cancer that was launched in December 2009. In addition the development of a certification programme for specialist breast units is proposed within the new cancer partnership and ED will work toward this in 2010. ED continues to add members from countries where services described in the EU Guidelines are not well known or available, so the challenge of educating advocates and health professionals concerning them is on-going. In September 2010 the European Commission has provided us with a grant to further educate our national leaders on these guidelines so that they can better advocate for these services in their countries. Nonetheless current surveys and research indicate there is still much to do before implementation is carried out in many countries.

Friday, 26 March 2010 18:15–19:15

POSTER SESSION

Locally advanced and metastatic disease

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Assessment of quality of life (QoL) in contemporary phase III trials in advanced breast cancer (ABC): is it worthwhile?

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Background: QoL parameters are often used as endpoints in phase III trials of systemic therapy for ABC. However, the extent to which this has been done in recent studies, as well as the frequency and correlates of significant gains in QoL, have not been assessed systematically.

Methods: We used the medical subject headings "breast neoplasms" and "drug therapy" to search PubMed for the main paper reporting phase III trials on system icantineoplastic therapies published between January 1, 1998, and July 15, 2009 in 11 leading medical journals (*Ann Oncol*, *BCRT*, *Br J Cancer*, *Cancer*, *Clin Cancer Res*, *Eur J Cancer*, *JCO*, *JNCI*, *Lancet Oncol*, *Lancet* and *NEJM*). We also searched for companion papers reporting on QOL separately. We excluded studies on high-dose chemotherapy, papers reporting combined analyses of two or more trials, and companion studies on correlative biology or prognostic factors.

Results: The search yielded 86 trials that enrolled a total of 33,669 evaluable patients in 192 trial arms, 2 of these arms with placebo/best supportive care alone (maintenance trials). QoL was mentioned/reported in the main paper in 34 trials, reported in a companion paper in 1 (a total of 35/86=41%), and mentioned in the abstract of the main paper in 19/34 cases (56%). The most common instrument used for QoL assessmentwas QLQ C-30. There was no temporal trend for reporting of QoL in the two 6-year periods ($P = 0.89$). Although formal statistical comparisons were reported in 31/35 cases (89%), a significant difference was found in only 4/31 (13%) trials, in all cases favoring the experimental arm (3 chemotherapy, 1 hormone therapy trial). Given the small number of studies with a significant QoL finding, we did not assess correlates for gain in QoL.

Conclusion: QoL has been assessed formally in nearly 40% of contemporary phase III trials in ABC. Although statistical analyses were performed in the vast majorityof those cases, a significant gain in QoL has been rare. QoL is one ofthe key indicators of treatment benefit for regulatory agencies, but contemporary systemic therapies for ABC do not appear to affect QoL differentially.

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A Belgian multicenter phase II randomized trial in HER2-negative metastatic breast cancer evaluating consolidation antiangiogenic therapy with sunitinib after objective response to taxane-based chemotherapy

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Background: We tested the hypothesis that antiangiogenic treatment with sunitinib is able to delay breast cancer progression after tumor mass reduction (objective response) induced by taxane-based chemotherapy, and describe adverse events and dose reductions.

Patients and Methods: This is a dual-arm open-label randomized multicenter phase II clinical trial with 2:1 randomization evaluating the efficacy of sunitinib (study arm A) versus no therapy (control arm B, only for descriptive purposes) in patients with metastatic breast cancer after objective response (PR or CR) to taxane-based chemotherapy. Eligible patients had metastatic HER2-negative breast cancer and objective response after 10−20 weeks of first- or second line taxane-containing chemotherapy. The primary endpoint was the proportion of patients alive and without disease progression (PFS) at 5 months after study entry in arm A. If $\leqslant$18/36 patients are progression-free and alive at 5 months, sunitinib will be declared insufficiently active (beta 0.05); if $\geqslant$22 patients are progression-free and alive at 5 months, sunitinib will be declared active (alpha 0.05) and it will be recommended to continue the trial as a phase III design.

Results: 10/36 patients (28%) reached 5 months PFS in arm A and 4/19 in arm B (21%). Median PFS was 2.8 months in Arm A and 3.1 months in Arm B. The outcome in arm A was far below the predefined threshold for moving into phase III. Because 53% (17/32) required dose reduction at a starting dose of 50 mg (4w on/2w off), the protocol was amended for a starting dose of 37.5 mg continuously, which resulted in 44% (7/16) dose reduction requirement. Most measured toxicities (all grades) were more common in arm A. Grade III-IV toxicity occurred in 69% of patients in arm A (mainly fatigue 31%, musculoskeletal pain 11%, neutropenia and thrombopenia 8%) and 11% in arm B.

Conclusion: This study does not confirm the hypothesis that sunitinib can lead to a clinically relevant and statistically significant proportion of patients with PFS of $\geqslant$5 months after objective response to taxanes. Sunitinib induces adverse events requiring dose reductions in half of the patients. This exploratory study does not support a role of consolidation therapy with sunitinib in this clinical setting.

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Locoregional treatment of inflammatory breast cancer after neoadjuvant chemotherapy

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Background: The aim of this retrospective, mono-centric, study was to assess the benefit of breast surgery for inflammatory breast cancer (IBC).

Material and Methods: From January 1st 1985 and December 31st 1999; out of 13180 patients diagnosed at the Institut Curie with non metastatic breast cancer, 280 (2%) were treated with curative intent for IBC with primary chemotherapy followed by either exclusive radiotherapy (118 patients, 51%) or surgery with or without radiotherapy (114 patients, 49%). Median follow-up of 11 years.

Results: The two groups were comparable apart from a fewer rate of tumors smaller than 70 mm (43% *vs* 33%, $p = 0.003$), a higher rate of clinical stage N2 (15% *vs* 5%, $p = 0.04$) and fewer histopathologic grade 3 tumors (46% *vs* 61%, $p < 0.05$) in the no-surgery group. The addition of surgery was associated with a significant improvement in locoregional disease control ($p = 0.04$). At 5 years locoregional free interval was 79% in the surgery group *vs* 66% in the exclusive radiotherapy group and at 10 years: 78% *vs* 59% respectively. In the univariate analysis, in addition to the absence of surgery ($p = 0.04$), other prognostic factors associated with higher locoregional recurrence rates were: high clinical nodal stage ($p = 0.009$), high histological nodal status ($p = 0.02$) and the

absence of taxanes in the neoadjuvant chemotherapy regimen (p = 0.02). In the multivariate analysis, only the clinical N2 stage was associated with a higher rate of locoregional recurrences. There were no significant difference in overall survival (52% at 5 years, 38% at 10 years, p = 0.32) or disease-free interval (at 5 years 32%, at 10 years 26%, p = 0.35). Factors associated in univariate analyses with a decreased overall survival were age over 50 years, the absence of achievement of a clinical response ⩾50%, absence of hormone receptors and the absence of taxanes in the neoadjuvant chemotherapy regimen. In multivariate analysis, only the absence of hormone receptors and either complete or partial clinical tumor response remained significant.

Factors associated in univariate analyses with a higher rate of disease recurrences were the absence of achievement of a clinical response ⩾50%, absence of hormone receptors and the absence of taxanes in the neoadjuvant chemotherapy regimen. In multivariate analysis, only the absence of hormone receptors and of clinical tumor response remained significant. Late toxicities were not significantly different between the two treatment groups except for a higher rate of fibrosis in the no-surgery group (p < 0.0001), and more lymphedema in the surgery group (p = 0.002).

Conclusion: Our data suggest an improvement in locoregional control in patients treated by surgery, in conjunction with chemotherapy and radiotherapy, for IBC. Efforts must be made to improve overall survival.

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Re-irradiation plus hyperthermia for recurrent breast cancer gives high local response and locoregional control

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Background: Locoregional recurrent breast cancer, especially in previous irradiated area, generally implies a poor prognosis. Treatment options are limited.

A cohort of 130 patients, treated in the AMC from 1982–2003, was analysed to evaluate the response and long term locoregional control and toxicity of re-irradiation (re-RT) and hyperthermia (HT) for locoregional recurrent breast cancer in previously irradiated area.

Patients/methods: Median age was 57 years. Median follow-up was 109.2 (63.0–187.2) months. All patients received extensive previous treatments, including surgery and irradiation to a median dose of 50 Gy in 5 weeks. Most (90%) received one or more lines of systemic therapy. Initial tumor stage included stage 1−4 (36, 50, 13 and 2%, respectively). Concurrent metastases occurred in 41 (32%) patients. Ninety patients (69%) had one or more previous locoregional recurrences before re-RT+HT. Median time interval between primary treatment and current recurrence was 36.9 (2.8–240.2) months. At start of re-RT+HT the median tumor size was 10 cm (0.5−30) and comprised >25% of the ipsilateral chest wall in 38% of patients. Thirty-five patients presented with lymphangitis cutis carcinomatosa and 38 with regional tumor activity. Recurrences were classified as single (n = 22), multiple (n = 60) or diffuse (n = 35).

Re-RT consisted of 32 Gy (15−40), given twice a week. Four (1−8) sessions of superficial hyperthermia were added once a week using CFMA-434 MHz applicators. Aim temperature was 41−43ºC for one hour. Concurrent chemotherapy was given in 22% and concurrent hormone therapy in 32% of patients.

Results: Overall clinical response rate, including regional disease, was 83% (CR+PR): 67 patients (52%) had a complete remission and 40 (31%) a partial remission. Fifteen (12%) patients showed no response and 2 had local progression. After CR the three-year local control rate was 38%. For the total cohort the three-year overall survival was 18%.

Most frequent acute toxicities were erythema and epidermolysis. Fibrosis was the most frequent late toxicity. Acute and late ⩾ grade 3 toxicity occurred in 26% and 16% of patients, respectively. One grade 5 (lethal) event occurred due to infection of a late radiation ulcer.

Discussion/Conclusion: The combination of re-irradiation and hyperthermia appears to achieve good locoregional control with an acceptable risk of side effects, particularly in view of the high tumour burden and resistance to previous treatments.

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Trends in survival in metastatic breast cancer

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Background: In the last 20 years new treatment options in breast cancer have evolved. We wanted to determine whether the survival of patients with metastatic breast cancer have improved during this period.

Materials and Methods: All pts with a diagnosis of disseminated breast cancer established 1985–2004 in the county of Kalmar were identified from the patients registry. Patient and tumour data was retrieved from patient records and the pathology database. Survival curves were constructed and median survival in months was determined for each 5 year interval 1985–2004 for the whole cohort and by grade. The percentage of patients surviving more than 2, 3, 5 and 10 years after first metastatic event was determined for each group. Separate analyses were performed for pts with ER/PR positive and HER2 positive tumours resp to determine whether the survival changed in the first 50% of the cohorts compared to the last.

Results: The median survival of the 557 pts in the whole study population was 10, 14, 16 and 22 months in each successive five-year period from 1985 to 2004.

For pts with grade 3 tumours (N = 288) the median survival increased from 10, 12, 15 to 17 months resp. The percentage of pts with grade 3 tumours surviving more than 3 years improved from 14 to 34% and the 5 years survival increased from 8 to19%.

The median survival for pts with grade 2 tumours (N = 168) was 17, 22, 23 and 27 months resp. The percentage of pts surviving more than 2 years increased significantly from 33 to 51%.

Only 43 pts had grade 1 tumours. The median survival for this group was 33 months and did not change.

ER/PR positive pts were 276. The median survival was 22 months and did not change over time. Sixty-four percent of pts diagnosed before 1997 survived more than 2 years and 44% more than 3 years. Corresponding figures for pts diagnosed 1997 and later were 68 and 48% resp.

Forty HER2+ pts treated before 2000 had a median survival of 14 months and the same number diagnosed year 2000 and onwards 21 months. Two-year survival improved from 20 to 43%, 3-year from 12 to 33 and 5-year survival from 5 to 15%. Fifty-eight of the HER2 positive tumours were of grade 3. In this subset 46% of pts diagnosed 2000 or later survived more than 2 years, 32% more than 3 years and 21% more than 5 years as compared to 10, 3 and 3% resp for those diagnosed before the year 2000.

Conclusions: Survival in metastatic breast cancer improved 1985–2004. The most striking improvement was achieved in the HER2 positive subset. The median survival of ER/PR positive patients did not increase.

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Circulating cross-linked N-telopeptide of type 1 collagen and VEGF in patients with bone metastases from breast cancer treated with zoledronic acid

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Background: Breast cancer is the most frequent tumor in women and 80% of patients with metastatic disease have bone metastases (BM), which are responsible for high morbidity and for reduced quality of life. Zoledronic acid (Zometa®, Zol), routinely used to treat patients with BM, inhibits bone resorption and has antitumor properties. It has also been reported to have an antiangiogenic effect.

Material and Methods: The present study evaluated serum levels of vascular endothelial growth factor (VEGF) and cross-linked N-telopeptide of type I collagen (NTX) in 31 consecutive patients with advanced breast cancer. Patients were eligible if they were at first diagnosis of bone metastases and if they had not previously undergone bisphosphonate treatment. All patients received the standard Zol schedule of a 4-mg infusion every 28 days. Patients were monitored for about 9 months and blood samples were collected before the first infusion of Zol and every 3 months thereafter.

Results: The baseline VEGF median value was 298 ng/ml (25–1264). The median value at 3 months was 345 ng/ml (62–977), 307 ng/ml (112–1307) at 6 months and 394 ng/ml (172–1004) at 9 months, none of which reached statistical difference. In contrast, NTX median values significantly decreased with respect to baseline (median value 16, range 3−45 nm BCE) at 3 (10 nm BCE, range 5−35) and at 6 months (10 nm BCE, range 5−21) (p < 0.001), but not at 9 months (12 nm BCE, range 5−45). The NTX serum median level at 3 months was 34% less than that of the baseline. Blood samples at 6 and 9 months showed a decrease of 38% and 26% with respect to baseline, respectively. There was no correlation between VEGF and NTX values.

Conclusions: The present work shows that standard monthly treatment with zoledronic acid induced a rapid and long-lasting decrease in NTX levels in the majority of patients, in marked contrast to literature data on urinary NTX in a similar patient setting. Conversely, no change was observed in circulating VEGF values, which may be due to the small cases series or to the fact that monthly treatments have less effect on VEGF than non standard weekly administration. The study is ongoing to validate these data.