5033 POSTER DISCUSSION

Secondary PROphylaxis with G-CSF has a major effect on delivered dose intensity: the results of the UK NCRI/Anglo Celtic SPROG trial for adjuvant chemotherapy of breast cancer

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Background: Chemotherapy-induced neutropenia frequently results in delays or dose reductions in subsequent cycles of therapy. Failure to deliver the planned dose intensity of adjuvant chemotherapy may compromise survival outcomes. We aimed to assess whether secondary prophylaxis with granulocyte colony-stimulating factor (G-CSF) can help to maintain chemotherapy dose intensity in patients with early breast cancer.
Patients and Methods: Between 2001 and 2007, 407 patients with early stage breast cancer receiving standard dose adjuvant chemotherapy were randomized at first neutropenia event (absolute neutrophil count <1000/mm^3 or neutropenic fever) to standard management with dose delays or dose reductions (control group) versus G-CSF as secondary prophylaxis (intervention group). The patients were well matched for the usual age demographics and 95% were receiving anthracycline or anthracycline-taxane sequential regimens. The majority of intervention patients (N = 129) received filgrastim for 7 days, but after it became available pegylated filgrastim (pegfilgrastim) was given to 75 patients. The primary endpoint was the proportion of patients achieving a relative dose intensity (RDI) of 85% or greater.
Results: In the control group (N = 203), only 45% of patients achieved 85% or more of planned RDI, whereas in the intervention group (N = 204), 75.8% achieved 85% or more planned RDI ($p < 0.01$). Randomization was performed for 42% of patients after the first cycle and for 73% within the first 3 cycles. The control data are similar to those reported by Lyman. After randomization, 64.9% of controls versus 17.5% of G-CSF intervention patients had a second neutropenic event ($p < 0.01$). A subgroup analysis showed a major benefit for pegfilgrastim compared with filgrastim in respect of the primary endpoint: 85.1% achieved 85% or greater RDI compared with 70.7% of patients who received filgrastim.
Conclusions: Secondary prophylaxis with G-CSF is necessary to guarantee the quality of chemotherapy dose intensity after a neutropenia-associated delay or febrile event has occurred.
This trial was supported by Amgen.

5034 POSTER DISCUSSION

Troponin I and C-reactive protein as biomarkers for changes in left ventricular ejection fraction in patients with early stage breast cancer treated with dose-dense doxorubicin and cyclophosphamide (AC) followed by weekly paclitaxel with trastuzumab and lapatinib

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Background: The incorporation of anti-HER2 agents into anthracycline-based chemotherapy potentially increases cardiotoxicity. Early detection of cardiotoxicity is limited to measuring changes in left ventricular ejection fraction (LVEF) at arbitrary time points, which has limited sensitivity and specificity. Cardiac Troponin I (TnI) is a highly specific marker of myocardial damage. C-reactive protein (CRP) is a sensitive inflammatory marker. Within a prospective study testing the feasibility of dose-dense (dd) AC – followed by weekly paclitaxel (P) with trastuzumab (T) and lapatinib (L), we included a pre-planned analysis of correlative TnI and CRP as early biomarkers of cardiotoxicity.
Materials and Methods: Patients (pts) with HER2+ early stage breast cancer were treated with ddAC (A 60 mg/m^2 + C 600 mg/m^2) $\times$4 then weekly P (80 mg/m^2) $\times$12 + T + L (1000 mg/day). T+L continued for a total of 52 wks. Pts had baseline LVEF $\geqslant$50%. Pts with unstable angina, CHF, recent MI, uncontrolled arrhythmia, grade 3 QT prolongation were excluded. LVEF was assessed by MUGA scan at mths 0, 2, 6, 9 and 18. TnI and CRP were measured every 2 wks during ddAC-PTL, then at mths 6, 9 and 18. Investigators were blinded to these results until pts completed 18mth follow-up (F/Up).
Results: 95 pts enrolled from Apr 07 – Apr 08. 39/95 (41%) withdrew due to PTL toxicities (incl. 3 asymptomatic LVEF decline and 3 CHF). As of Apr '09 37 pts have completed 18 mths F/Up; none of whom had CHF or LVEF decline <50%. At baseline all available TnIs were <0.06 ng/ml. During treatment 22/37 pts (59%) had elevations in TnI. 21 pts had minimal elevations (<0.31 ng/ml). 1 pt had elevated TnI above normal range (>0.31 ng/ml) with AC#4. MUGA 1 wk later was unchanged (LVEF 75%) but she died from sepsis during subsequent treatment without evidence of CHF. Of 22 pts with elevated TnI, 4 had LVEF decline >10% and 9 had LVEF decline 5 $\leqslant$10%. Only 3 of 15 pts (20%) with TnI <0.06 ng/ml had LVEF decline >5%. Elevations in TnI occurred only during chemotherapy and no pt had a TnI > 0.06 ng/ml during TL or at 18 mth F/up. At baseline 29/37 pts (78%) had normal CRP (<0.8 mg/dl). Elevations in CRP (>0.8 mg/dl) occurred in 29/37 (78%) pts during chemotherapy but only in 8/37 (22%) pts during TL or at 18 mth F/Up.
Conclusions: Fluctuations in TnI and CRP are common in pts with normal LVEF receiving ddAC-PTL and may correlate with subtle declines in LVEF. These abnormalities do not persist after chemotherapy during TL. Updated results will be presented including pts with CHF and LVEF < 50%.

5035 POSTER DISCUSSION

The patient's anastrozole compliance to therapy programme (PACT): evaluating the influence of a standardized information service on compliance in postmenopausal women with early breast cancer

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Background: Little is known about compliance to aromatase inhibitors and patient motivation outside of clinical trials and the effect of compliance on patient outcome. Retrospective pharmacy data suggest that within the first year of therapy early breast cancer patients' pick-up rate of prescribed aromatase inhibitor packs drops below 70%. The PACT study investigated if standardized continuous information about drug treatment would affect patients' compliance and improve clinical outcome in postmenopausal women with early-stage breast cancer receiving adjuvant anastrozole.
Material and Methods: The PACT programme is a two arm, randomized trial with a primary duration of 12 months and follow-up extended to 60 months. Following consent, postmenopausal women with hormone receptor positive early breast cancer receiving anastrozole as adjuvant treatment were randomised to routine clinical care alone or to receive additional standardized information, consisting of 9 mailings of brochures and letters over the first 12 months following initiation of therapy. Primary endpoint is compliance rate in the standard versus intervention arm after 12 months, secondary endpoints include safety, reasons for non-compliance, influence of baseline characteristics on compliance, and influence of compliance on clinical outcome parameters. Compliance was defined by an 80% intake of the total medication and was evaluated by patient self-reporting via standardized questionnaires, cross-checks of prescription data from hospital records and physician recall. QoL and patients' satisfaction are assessed with standard questionnaires.
Results: From October 2006 to November 2008, 4924 patients were enrolled. Demographic data and baseline characteristics including median age, disease parameters, BMI, QoL at study start, co-morbidities and concomitant medication will be presented.
Conclusions: As of today, PACT is the largest prospective investigation on compliance with aromatase inhibitor therapy. It will provide valuable insights into the reasons for non-compliance to adjuvant AI therapy and demonstrate if a simple intervention such as standardized written information throughout the first treatment year may improve compliance and hence patient outcome.