of paclitaxel and trastuzumab. Cycle 4 consisted of trastuzumab alone. A healthy male child was delivered and at 3 year follow-up is developmentally normal. Pt achieved yPT0N2, and has since developed metgastatic BC.
Case 2: A 38 year old mother was 32 weeks pregnant at diagnosis with LABC. She was treated with neo-adjuvant docetaxel, cyclophosphamide and trastuzumab (one cycle) followed by one cycle of trastuzumab alone. Pt achieved yPT3N0 A healthy baby was delivered and is now a developmentally normal 12 month old child. Clinical cardiac dysfunction was not observed in either mother during the described pregnancies.
Conclusion: In these 2 cases induction regimens incorporating trastuzumab, administered during the second trimester, were not associated with either maternal or fetal adverse cardiac sequelae. The paucity of cases reported in the literature, the established concerns of non-cardiac adverse sequelae and preclinical studies demands cautious in the use of trastuzumab in pregnant patients.

5154 POSTER

Adjuvant Treatment of Breast Cancer With FEC-D − a Retrospective Analysis of a Single Portuguese Cancer Centre Database

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Background: Adjuvant chemotherapy (CT) with 3 cycles of fluorouracil, epirubicin and cyclophosphamide (FEC) followed by 3 cycles of docetaxel (D) was shown to significantly improve disease-free and overall survival in node-positive breast cancer. Our purpose was to evaluate the toxicity profile, hospital admissions and non-programmed visits in patients (pts) on treatment with adjuvant FEC-D.
Methods: We retrospectively reviewed all cases of breast cancer pts treated with adjuvant FEC-D. Blood count values were registered on cycle's D_1, on hospital admission and on non-programmed visits. Left ventricular ejection fraction (LVEF) was measured at baseline and after FEC. Toxicity was evaluated using Common Terminology Criteria version 3. Differences between pts who were hospitalized or who had non-programmed visits were assessed with parametric and non-parametric tests as appropriate.
Results: From November 2007 through June 2009, 414 pts were treated with FEC-D. All were female with median age of 52 years (range 24−80; 19% $\geqslant$ 65 years), 92% had ECOG 0 and 65% presented no co-morbidities. Over 98% of pts completed 6 CT cycles. A relative dose-intensity (RDI) of FEC >96% was achieved in 75% of pts and 71% of pts accomplished a docetaxel's RDI of $\geqslant$90%. Most common severe adverse events (SAE) were febrile neutropenia (FN) in 14% of cases, neutropenia on D_{21} of CT cycle (12%) and mucositis (3%). Median baseline LVEF was 65% and a LVEF reduction of >10% after FEC was observed in 11%. One pt had an acute coronary syndrome. There were 113 non-programmed visits with the main causes being infection (31%) and FN (21%). Hospitalizations were 52, being FN and infection the main causes (69% and 17%; respectively). Age or the presence of co-morbidities had no impact on hospital admissions or non-programmed outpatient visits ($p > 0.05$). RDI for both FEC and D were lower in hospitalized pts compared to those who were not ($p < 0.005$). In the case of non-programmed visits, the same was true for docetaxel's RDI ($p = 0.003$).
Conclusion: Adjuvant FEC-D was shown to have a favorable safety profile. Our study found myelosupression and mucositis as the most frequent toxicities. RDI reductions in the groups of hospitalized pts and those who attended non-programmed consultations reflect the occurrence of toxicity. Docetaxel accounted for more severe cases of febrile neutropenia leading to more hospitalizations and lower RDI, which was, nevertheless, $\geqslant$ 90%. in most pts.

5155 POSTER

Reduction in Fractures Following Adjuvant Zoledronic Acid in Stage II/III Breast Cancer − the AZURE Trial (BIG 01/04)

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Background: The AZURE trial is an academic study designed to determine whether zoledronic acid (ZOL) added to standard adjuvant therapy (Control) reduces the risk of recurrence and improves survival in patients with stage II/III breast cancer. We report here the impact of ZOL on fractures.
Materials and Methods: 3360 pts were randomized to receive (neo) adjuvant chemotherapy (CT) and/or endocrine therapy +/− ZOL 4 mg iv every 3−4 weeks for 6 doses, then 3 monthly $\times$ 8 and 6 monthly $\times$ 5 to complete 5 years treatment. Patients (pts) with osteoporosis and those using bisphosphonates, either at baseline or in the previous year, were excluded from study entry.
Results: Patient and treatment characteristics were well balanced. 3208 pts (96%) received (neo) adjuvant CT. With a median follow-up of 59 (IQR 53.2–60.9) months, there have been 752 DFS events. ZOL had no overall effect on DFS (adjusted HR = 0.98, 95% CI 0.85–1.13; p = 0.79). Only 146 of 1678 (8.7%) control pts received a bisphosphonate prior to a disease-free survival (DFS) event.
Fractures occurred in 152 (4.5%) study pts; 60 of 1681 (3.6%) ZOL pts experienced 65 (range1−3) fractures, compared with 92 of 1678 (5.5%) control pts with 110 (range 1−4) fractures (difference −1.9%; 95% CI −3.3%, −0.5%). There was substantial protection from axial fractures with ZOL (eg spine 2 vs.18; femur 1 vs. 4) compared to appendicular sites (eg wrist 6 vs.7; hand 3 vs.0). Trauma was recorded as causal in 42 of 65 (64%) fractures in the ZOL group and 51 of 110 (46.4%) in the control group. There were no reports of atypical femoral fractures with ZOL. Fifty six (86.2%) of the fractures in the ZOL group and 68 (61.8%) in the control group occurred in the absence of, or prior to a DFS event. The non DFS event associated fracture rate was 3.0% (51 pts) in the ZOL group and 3.4% (57 pts) in the control group (difference −0.4%; 95% CI −1.6%, 0.8%). In contrast, 0.5% (8 pts) and 2.0% (34 pts) in the ZOL and control groups respectively experienced a fracture after a DFS event (difference −1.6%; 95% CI −2.3%, −0.8%). For pts with a DFS event, the fracture rate was 2.1% (8 of 377) for the ZOL group vs. 9.1% (34 of 375) of the control pts, with the majority of fractures occurring after a skeletal recurrence; 87.5% (7 of 8) ZOL and 88.2% (30 of 34) control pts.
Conclusions: Adjuvant ZOL given in the schedule utilised in AZURE reduced the fracture rate in patients with breast cancer, particularly following a DFS event, and despite the use of bisphosphonates after development of bone metastasis.

5156 POSTER

ABCB1 Single Nucleotide Polymorphismas a Possible Prognostic Factor in Breast Cancer Patients Receiving Docetaxel and Doxorubicin Neoadjuvant Chemotherapy on Systemic Treatment

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Background: Expression of the adenosine triphosphate-binding cassette B1 (ABCB1) transporter and P-glycoprotein are associated with resistance to anticancer drugs. The purpose of this thesis was to investigate the role of single nucleotide polymorphism (SNP) in the ABCB1 and CYP3A genes in breast cancer patients who were treated with neoadjuvant docetaxel and doxorubicin chemotherapy.
Material and Methods: Patients with histologically confirmed breast cancer, Stage II or III, referred for neoadjuvant chemotherapy were enrolled. Patients were treated with 3 cycles of neoadjuvant and adjuvant chemotherapy with docetaxel and doxorubicin. The polymorphisms of ABCB1 (C3435T, G2677T/A, and C1236T) and CYP3A were genotyped. The correlation of genetic polymorphisms of ABCB1, CYP3A, and clinical outcomes was analyzed.
Results: Between September 2003 and September 2008, a total of 216 patients were enrolled. *ABCB1 3435*TT genotype had a longer OS than CT/TT. With univariate analysis of the overall survival (OS), good performance status (PS), invasive ductal carcinoma, initial operable stages, estrogen receptor-positive, non-triple negative, and the TT genotype of *ABCB1* C3435T were associated with a lower risk of death. Multivariate analyses for the OS revealed that PS, initial clinical stage, and triple negative phenotype were significantly associated with the OS. *ABCB1 3435*TT genotype was also associated with a lower risk of death with marginal significance ($p = 0.071$). *ABCB1 3435*TT genotype had a higher AUC than CC/CT genotype for docetaxel ($p = 0.031$). These higher AUCs in the C3435TT genotype was associated with increased toxicities of neutropenia ($p = 0.037$) and diarrhea ($p = 0.017$).
Conclusions: In conclusion, this study showed that the genetic polymorphism of ABCB1 C3435T might be associated with a longer OS. Our results also suggest that the prediction of docetaxel toxicity might be possible for ABCB1 C3435T polymorphism. Larger prospective studies as well as functional studies in human subjects are warranted.