with breast cancer undergoing adjuvant or neoadjuvant anthracyclin-based chemotherapy with or without docetaxel.
Material and methods: we studied the incidence and the reversibility of clinical amenorrhea induced by different chemotherapy regimens: i) 6 cycles of 5-fluorouracil 500mg/m2, epirubicin 100mg/m2 and cyclophosphamide 500mg/m2 on day 1 every 3 weeks (6FEC) and ii) 3 cycles of FEC 100 followed by 3 cycles of docetaxel 100 mg/m2 on day 1 every 3 weeks (3FEC/3D) and iii) 4 cycles of FEC 100 followed by 4 cycles of docetaxel on day 1 every 3 weeks (4FEC100/4D) .Recovery of ovarian function was defined as recovery of premenopausal hormonal values :luteinizing hormone (LH <17mIU/ml),follicle-stimulating hormone (FSH <45.7mIU/Ml) and oestradiol (E2>50pg/ml).This recovery of ovarian function did not need to be associated with regular menses.Hormonal dosages were performed every 3 months starting at the beginning of chemotherapy and during the year following the end of chemotherapy.After, dosages were performed every 6 months.
Results: 170 premenopausal patients were included between january 2005 and january 2008: 62 patients received 6FEC, 66 patients 3FEC/3D and 42 patients 4FEC/4D. The median age was 41 years (range: 25-51) in 6FEC, 42.8 years (range: 27-52.8) in 3FEC/3D and 40.2 years (range: 24-49.5)in 4FEC/4D. The incidence of chemotherapy-related amenorrhea at the end of chemotherapy was similar in the 3 groups: 90.3% in the 6FEC arm, 89.4% in the 3FEC/3D arm and 92.8% in the 4FEC/4D arm. However in the year following the end of chemotherapy, more patients recovered ovarian function in the 3FEC/3D arm (51.5%)(p=0.017) and in the 4FEC/4D arm (50%)(p=0.046)compared with the 6FEC group (30.6%). The difference was statisticaly significant for patients > or=40 years but not for patients < 40 years.Importantly, among the 23 patients with premenopausal hormonal values and treated with tamoxifen, 12/23 did not mention any menses recovery during the first year of follow-up.
Conclusion: our prospective study confirms our previous retrospective data showing that 3FEC/3D and 4FEC/4D induce less definitive amenorrhea than 6FEC. Age is the most important predictor of ovarian function recovery, independently of chemotherapy regimen.Anamnestic data, especially in patients treated with tamoxifen are insufficient to determine pre-or postmenopausal status. Therefore, hormonal values must be followed regularly during and after chemotherapy. Since the menopausal status has an impact on the endocrine therapy choice.

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Incidence of Febrile Neutropenia with Taxane-Based Systemic Therapy in Women with Early Stage Breast Cancer.

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Background: Febrile neutropenia (FN) is one of the most significant toxicities experienced by patients treated with systemic therapy. Taxanes now play an integral role in the systemic therapy for women with early stage breast cancer. The most common taxane-containing regimen utilized in Ontario, Canada is 5-Fluorouracil/Epirubicin/Cyclophosphamide x 3 followed by Docetaxel x 3 (FEC-D). PACS 01 reported a febrile neutropenia (FN) rate of 11.2% in the FEC-D arm. In our clinical practice, clinicians have noted a much higher rate of FN. We report the FN rate with the use of FEC-D in women with early stage breast cancer treated at tertiary care centers in Ontario.
Methods: All women with early stage breast cancer who were treated with FEC-D from three tertiary care cancer centers in Ontario, Canada (London, Sudbury, Ottawa) between June 2006 and December 2008 were included in this retrospective analysis. Data included: demographics, staging, hormone receptor status, primary prophylaxis use with growth factors, FN rate, admission to hospital and duration of hospital admission.
Results: Median age of 630 women is 52 years (r: 24-77). Staging was: I (88), IIA (243), IIB (159), IIIA (94), IIIB (23), IIIC (14) and 9 unknown. A total of 474 (75.2%) were ER positive. Primary prophylaxis with growth factor support was given to 222 patients (35%) and 408 patients (65%) did not have upfront prophylaxis. Of the 222 patients who were given primary prophylaxis, 14 patients (6.3%) were diagnosed with FN. Of the 408 patients who did not receive primary prophylaxis, 120 patients (29.4%) were diagnosed with FN. All patients (n=120) diagnosed with FN received secondary prophylaxis with growth factor support. A total of 126 patients (20%) were admitted to hospital for FN. The median duration of hospital admission was 3.9 days (r: 1-65 days). The impact of risk factors, the use of filgastrim versus pegylated filgastrim on FN rates and the clinical ramifications of febrile neutropenia (ICU admissions/deaths) will be reported.
Conclusions: The results of this retrospective analysis demonstrate a much higher risk of FN (29.4%) with FEC-D than has been previously reported. More complete reporting of primary prophylaxis is required. This rate of FN would warrant use of primary prophylaxis for patients prescribed FEC-D, particularly in high risk subgroups.

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Changing Therapy as a Consequence of the Behaviour of CETC during Adjuvant Trastuzumab Treatment in Patients with Her2/Neu Positive Breast Cancer.

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Gene silencing, demethylation, translocations and amplifications crucially contribute to the growth potential and aggressiveness of malignant tumors. This has led to the development of compounds specifically targeting such alterations. Although parts of these compounds have led to an impressive improvement in relapse free survival such as trastuzumab in breast cancer treatment, a considerable part of patients carrying the alteration will not respond to this targeted treatment. Therefore, in addition to defining the subpopulation of patients with a high probability of responding to the targeted therapy only immediate control of the response to treatment will ultimately improve outcome.
Epithelial tumor cells circulating in peripheral blood are easily accessible and have been shown to reflect the response of the tumor to therapy. They can, therefore, be used to monitor the effect of therapy.
Here we report on the application of therapy monitoring using CETCs during adjuvant trastuzumab treatment and the consequences which may be deduced from these observations for individualized therapy.
30 patients with either IHC3+ or FISH confirmed Her2/neu positive breast cancer were prospectively analysed for the number of CETC before therapy, before each new cycle of chemotherapy and during maintenance therapy with trastuzumab.1ml of blood was drawn into EDTA vials, red blood cells lysed and the white blood cell pellet stained with FITC-labelled anti-Epcam. Green fluorescent cells were detected by image analysis and dead cells excluded due to red PI fluorescence.
Most patients showed the typical response of high risk patients upon chemotherapy with an initial decrease in cell numbers followed by a rapid reincrease still during chemotherapy. The subsequent maintenance therapy with trastuzumab led to a stabilization or a decrease in CETC numbers in 89% of patients all of which are in sustained complete remission whereas all of the 11% patients with increasing CETCs have suffered relapse. Thus CETC monitoring allowed an excellent discrimination of patients at risk of relapse also during trastuzumab treatment.
To further investigate the reason for treatment failure in the patients with increasing CETCs the cells were additionally analysed for their status of Her2/neu amplification during treatment. At the end of chemotherapy cells with a low number of Her2/neu amplificates comprised between 80 and 100% whereas cells with more than 10 signals comprised between 0 and 20%. During the subsequent therapy with trastuzumab the fraction of cells with more than 10 signals continuously increased to between 50 and 60%. This indicates that in these patients trastuzumab was not capable of eliminating the cells with a high Her2/neu amplification probably because the concentration of trastuzumab is not sufficient to eliminate these cells. With regard to the high probability with which a relapse must be expected in these patients a trial using higher trastuzumab doses seems warranted in patients with increasing CETC during the conventional trastuzumab treatment. Alternatively lapatinib might be an option.

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Real-Life Implementation of Treatment Guidelines for Adjuvant Chemotherapy in Invasive Breast Cancer: Retrospective Analysis of a Large Single Centre 10-Year Database.

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Background and objective: Decision to administer adjuvant chemotherapy to N-/M- invasive breast cancer (IBC) patients remains a clinical challenge. Several patient-related factors, such as age, tumor size and grade, or hormone receptor (HR) and HER2 status are incorporated in treatment guidelines. Recommendations have become more complex with time and availability of additional tests. Using the breast cancer database developed at Institut Paoli Calmettes (IPC) from 1999 onwards, our objective was to analyze the