Conclusion: In this cohort of MBC, high levels of Ki67 on the site of first relapse are significantly associated with a shorter survival. Despite the small sample size, this study represents the first evidence for the prognostic role of Ki67 in the metastatic setting. Correlation with gene expression profiles of the primary tumor and analysis of a larger independent cohort to confirm these findings are ongoing.

PO49

OVEREXPRESSION OF THE ONCOPROTEIN HER2 IN BREAST CARCINOMA IN A POPULATION OF YOUNG WOMEN IN WESTERN ALGERIA

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Introduction: In west of Algeria , the incidence of breast cancer increased by 19.5% from 1996 to 2004. With a standardized incidence of 36.9 / 100,000. Invasive ductal carcinoma is the most histologic type as found.
The HER family (Humen Epithelial Receptor), consisting of four members, HER2, is characteristic of receptor tyrosine kinase plays a fundamental role in the development and / or the growth of many human cancers.
Evaluation of overexpression and quantification of the HER2 protein in situ can target HER2 + patients may benefit from specific therapy (Herceptin - Trastuzumab-).
Immunohistochemical technique allows the identification and location of the overexpression of HER2 protein with the visualization of the target molecule on fixed tissue embedded in paraffin, taking into account that tumor cells invasive HER2 +.
Patients and methods: Our study, include 134 young women with invasive breast cancer, is realized from June 2007 to January 2011 at Oran CHU , anatomopathology laboratory and in developpement biology and differentiation laboratory. The aim of this work is the determination of clinicopathologic and biologic carcteristics of invasive brest carcinoma HER2+ in young women of west Algeria.
Results: The status of the HER2 oncoprotein highlighted by the antibody DAKO: with HER2 (score 0 and 1) 51.67%, HER2 (score 2 +) 6.05 %, HER2 + (3 + score) 43.28%, age of these patients is between 20 and 50 years (mean age 40 $\pm$ 05.03 years), the right breast is the site most affected (79%), the upper outer quadrant is the location found most (57%). Postsurgical size pT2 (69%), poorly differentiated tumors and undifferentiated G (77%), the SBR grading II & SBR III (80%), the invasion of axillary nodes N + (72%). The hormone receptor status identified by antibodies DAKO: RE-(77%), PR-(66%) & ER-PR- (62%).
Conclusion: HER2 overexpression has three interests: pejorative prognostic value, predictive value and requirements for the treatment of invasive breast cancers.
Only patients whose tumors over-express HER2 (score 3 + score 2 + and confirmed by FISH) may benefit from targeted therapy with trastuzumab.

PO50

E-CADHERIN IN METASTATIC AND NON METASTATIC BREAST CARCINOMA

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E-cadherin cell-cell adhesion molecule is important in carcinoma development and progression. Histopathological grade also has a role in prognosis of breast cancer. We conduct a study to determine wether loss or lower expression of E-cadherin related with grade of tumor can predict metastatic potential in invasive ductal carcinoma.
Immunohistochemistry was used to detect E-cadherin in metastatic and non-metastatic invasive ductal carcinoma in 20 sample of each group. We use clinical and chest x-ray, liver ultrasound, and bone scan to detect and determine metastases. Median age is 51.65 in metastatic group and 47.70 in non metastatic. In metastatic group there were 0 grade I, 10 grade II and 10 grade III. And in non metastatic there are 2 grade I, 9 grade II and 9 grade III. The negative expression of E-cadherin were found in 13 cases; 9 in metastatic and 4 in non-metastatic group. Low expression of E-cadherin is in 8 cases; 2 in metastatic and 6 in non-metastatic group. And there were 19 cases still express E-cadherin; 9 in metastatic and 10 in non metastatic cases.
Loss or lower expression of E-cadherin also occur in low grade tumor, but there are no statistically significant relation between tumor grade and loss expression of E-cadherin. E-cadherin expression is not significantly different between metastatic and non metastatic group, altough there is a trend to lower or loss expression in metastatic group.

PO51

CORRELATION BETWEEN GRP 78 EXPRESSION WITH NEOADJUVANT CHEMOTHERAPY AT LOCALLY ADVANCED BREAST CANCER

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Incidence of locally advanced breast cancer in Indonesia is higest among others and more increasing each year. One of therapeutic modality of locally advanced breast cancer is neoadjuvant chemotherapy, aim to eliminate cancer cells through intrinsic mechanism the apoptosis
GRP 78 has correlation with apoptosis mechanisms, whereas high GRP 78 expression indicates immortality of the cell to all apoptosis signaling.
The aim of this study was to understand the coreraltion of GRP 78 expression with response of FAC neoadjuvant chemotherapy in patient with locally advanced breast cancer.
This was cross-sectional study with a prespective observation, which included 37 locally advanced breast cancer patients who treated at Depatement of Surgical Oncology, Dr Hasan Sadikin Hospital Bandung / Faculty of Medicine, Padjadjaran University, during January 1st until December ^{31st} 2009. Evaluation response of neoadjuvant chemotherapy was performed, so was IHC examination of parafine block from incisional biopsy prior to administration of neoadjuvant chemotherapy to obtain information of GRP 78 expression.
The result of this study, there was significant correlation of GRP 78 expression with FAC neoadjuvant chemotherapy response in patient with locally advanced breast cancer ($p = 0.028$)

Clinical research

OR52

WHICH BENEFIT FROM SUBSEQUENT CHEMOTHERAPY LINES BEYOND THE SECOND FOR WOMEN WITH METASTATIC BREAST CANCER? EVIDENCE FROM A SINGLE-CENTER RETROSPECTIVE ANALYSIS OF SURVIVORSHIP

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Background: Although the true impact of chemotherapy (CT) in metastatic breast cancer (MBC) is still debated, in the routine clinical practice an increasing number of women asking for further treatment after progression receive subsequent CT lines. This study aimed to assess

which benefit could be brought by the succession of CT lines in patients treated for MBC and to identify women who benefit from these treatments.

Methods: This retrospective analysis included 980 women treated with CT for MBC at our Institution over a 7-year period (May 1999-July 2006). With overall survival (OS) data updated at December 1, 2008, the median follow-up was 125 months (range 48-192), OS and time to treatment failure (TTF) were calculated according to the Kaplan-Meyer method for each CT line. Cox proportional hazards model was used to identify factors that could influence TTF and OS.

Results: Median OS evaluated from day 1 of each CT line decreased with the line number from 34.8 months (980 patients, 1st line, range 4-208) to 22.6 months (838 patients, 2nd line), 14.6 months (684 patients, 3rd line), 12.4 months (302 patients, 4th line), 9.4 months (88 patients, 5th line), 8.2 months (45 patients, seven or more lines). Median TTF ranged from 9.2 months to 7.8 and 6.4 months for the first, second and third line, respectively, with no significant decrease observed beyond the 3rd line (median 5.2 months, range 4.8-6.2). In univariate analysis factors positively linked to a longer duration of TTF for each CT line were positive hormonal receptor status, absence of liver metastasis, adjuvant CT exposure, response to CT for the metastatic disease; in the multivariate analysis the duration of TTF for each CT line was the only one factor with significant impact on survival benefit for subsequent treatments ($p<0.001$).

Conclusions: CT beyond the 2nd line may be beneficial in a significant subset of women treated for MBC, with improved TTF and OS. These findings could help physician in planning an appropriate strategy of subsequent schedules for women with symptomatic MBC who responded to their 1st line CT, while non responder patients should be considered for clinical trials.

BP53

BOLERO-2: EVEROLIMUS IN COMBINATION WITH EXEMESTANE IN THE TREATMENT OF POSTMENOPAUSAL WOMEN WITH ESTROGEN RECEPTOR-POSITIVE ADVANCED BREAST CANCER REFRACTORY TO LETROZOLE OR ANASTROZOLE

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Background: The PI3K/Akt/mTOR pathway, a key regulator of cellular proliferation, metabolism, and angiogenesis, is constitutively activated in aromatase inhibitor–resistant breast cancer. Everolimus (EVE), an inhibitor of the PI3K/Akt/mTOR pathway has been found in phase II studies to be effective in combination with endocrine therapy to treat patients with estrogen receptor–positive (ER+) breast cancer who progressed while receiving nonsteroidal aromatase inhibitors. This multinational, double-blind, placebo-controlled phase III study (clinicaltrials.gov: NCT00863655; Trial Sponsor: Novartis Pharmaceuticals) evaluated EVE in combination with exemestane (EXE) in patients with ER+ advanced breast cancer (ABC) refractory to letrozole or anastrozole.

Methods: Postmenopausal women $\geq$18 years old with ER+ ABC whose disease was refractory to letrozole or anastrozole and who had a documented recurrence or progression were included. Patients were stratified by sensitivity to prior hormonal therapy and the presence of visceral metastasis and randomized (2:1) to EVE (10 mg daily) or matching placebo orally once daily, with both arms receiving EXE (25 mg daily). Treatment was continued until disease progression or unacceptable toxicity occurred. Primary endpoint was progression-free survival (PFS), assessed by the investigators. Secondary endpoints included survival, response rate, and safety. PFS was evaluated using Cox regression. A preplanned interim analysis was performed and reviewed by the independent data monitoring committee (IDMC) after observing 359 PFS events.

Results: 724 patients were randomized between 06/2009 and 01/2011 from 24 countries (485: EVE+EXE; 239: EXE). Baseline characteristics were well balanced; median age was 62 years, 56% had visceral involvement and 84% were sensitive to prior hormone therapy. Previous therapy included letrozole or anastrozole (100%), tamoxifen (48%), fulvestrant (16%) and chemotherapy (68%). At the interim analysis, the IDMC disclosed that the trial met its primary endpoint, as assessed by local investigators (HR: 0.43 [95% CI: 0.35-0.54], median 6.9 *vs* 2.8 months; $p=1.4\times10^{-15}$) and that results were consistent across the various subgroups. PFS analysis based on central assessment was also significant (HR: 0.36 [95% CI: 0.27-0.47], median 10.6 *vs* 4.1 months; $p=3.3\times10^{-15}$). Both analyses crossed the pre-specified thresholds for significance based on alpha-spending function using O'Brien-Fleming boundaries. Response rates were 9.5% and 0.4% on the EVE+EXE and EXE arms, respectively, $p<0.0001$. Most common grade 3/4 adverse events were stomatitis (8% *vs* 1%), anemia (5% *vs* <1%), dyspnea (4% *vs* 1%), hyperglycemia (4% *vs* <1%), fatigue (3% *vs* 1%) and pneumonitis (3% *vs* 0%) for the EVE+EXE and EXE groups, respectively.

Conclusion: EVE, when added to an aromatase inhibitor, significantly improves PFS and response rate and has a manageable safety profile. EVE in combination with an aromatase inhibitor is a new therapeutic option for women with previously treated ABC.

PO54

TREATMENT OF LOCALLY ADVANCED BREAST CANCER: A TUNISIAN EXPERIENCE

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Locally advanced breast cancer is defined by presence of primary tumor larger than 5cm with or without chest-wall or and skin involvement or clinically N3 axillary lymph nodes. Standard treatment includes primary chemotherapy followed by radiotherapy with chemotherapy and or hormonal therapy. The aim of this study was to present outcomes of LABC patients who received such sequence of treatment. A prospective collected data were retrospectively analyzed over a 5 years period from 2003 to 2008.Statistical methods included Kaplan Meier and Cox regression. 135 patients were initially involved but only 110 patients completed the described treatment sequence were evaluated. 15 patients (13.6%) were given Tamoxifen as adjuvant therapy. 11 patients (10%) had complete pathological response, 15 (13.6%) a complete clinical response. The 5-year survival is 47.2 % complete pathological response and clinical responses were identified by logistic regression to be the most important prognostic factors.

PO55

THE ROLE OF IN-VITRO HIGH RESOLUTION MAGIC ANGLE PROTON MAGNETIC RESONANCE SPECTROSCOPY (HRMAS) IN BREAST CANCER-A PILOT STUDY

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