that have previously been shown to correlate with toxicity/outcome in small patient groups receiving at least one of the FEC compounds (ABCBI/MDRI, ABCC1/MRP1, ABCC2/MRP2, ABCG2, ALDH3A1, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP3A5, DPYD, GSTP1, MTHFR, NQ01, TYMS, XPD/ERCC2, XRCC1). Secondly we investigated previously not studied genes known to be involved in epirubicin metabolisation (UGT1A1, UGT1A6, UGT2B7).

Material and Methods: We identified 1089 breast cancer patients treated in a single centre with 3 to 6 cycles of (neo-)adjuvant FEC (fluorouracil 500, epirubicin 100, cyclophosphamide 500 mg/m^2) from 2000–2010 for whom germline DNA is available. All patients were retrospectively evaluated through electronic chart review for all related non hematological grade 3−4 events (diarrhea, mucositis, myalgia, allergy, fatigue, nausea and vomiting). For statistical evaluation, correction was made for number of planned cycles, age and body mass index using logistic regression analyses. Because of multiple testing the false discovery rate (FDR) was calculated.

Results: Grade 3−4 non hematological events occurred in 43 out of 1089 patients (4%) (diarrhea 7/43, mucositis 8/43, myalgia 2/43, allergy 1/43, fatigue 7/43, nausea and vomiting 20/43). Homozygous (CC, 10%) and heterozygous (AC, 43%) variant genotypes for rs1801131 in the MTHFR gene, compared to the wild-type (AA, 47%) were significantly associated with all related non hematological grade 3−4 events (7.0 vs 4.8 vs 2.4%, p-value 0.033, FDR 0.72).

None of the other SNP could show a significant association (more details on other SNP and subcategories of endpoints will be presented at the meeting).

Conclusions: Genetic variation in a large set of candidate genes could not predict non hematological severe toxicity. The association found in the MTHFR gene was only moderately and with a high FDR. This is by far the largest breast cancer cohort in which the impact of genetic variability on toxicity was investigated.

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Inflammatory Breast Cancer, Moroccan Study

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Background: Inflammatory breast cancer (IBC) is characterized by a particular geographic distribution, being described as more common in the region of North Africa with 5−7% incidence.

IBC present specific histological and biological characteristics compared to non-inflammatory breast cancer.

It's an aggressive form of breast cancer, with poor prognosis: 5-year overall survival reached only 20−30% with a multimodal treatment for localized disease.

Material and Methods: The authors collected the cases of IBC diagnosed and treated at the institute during four years; they analyzed the epidemiology, clinical presentation, histological characteristics, treatment, and therapeutic results.

The diagnosis of IBC was clinical according to the AJCC (American Join Cancer Committee) definition. Maximal delay for inflammatory symptoms was 6 months to eliminate locally advanced pseudo inflammatory breast cancer: T4b with inflammatory aspect.

Results: From January 2005 to December 2008, we collected 172 cases of IBC (T4d) from 3400 new cases treated at the institute, representing 5%.

The median age was 46 years and 62% of the patients were inferior to 50 years.

73% presented clinical lymph nodes involvement and 27% was initially metastatic.

SBR (Scarff Bloom Richardson) was grade 1 in only 5.8% of cases. When performed, Estrogen receptors (ER) were negative in 51%, and HER2 was positive in 59%.

After Neoadjuvant chemotherapy for localized disease, 75% of the patients presented clinical objective response (cOR); 5.6% presented pathologic complete response (pCR) on the breast according to Chevalier grading, and only 2.1% on both breast and axillary lymph nodes.

Median progression free survival (PFS) and overall survival (OS) were respectively 12.4 and 15.8 months; 3-year PFS and OS were respectively 8% and 6.1%.

Statistical study found only negative ER and initial metastasis as predictive factors for worse OS and PFS.

Conclusion: IBC is an aggressive form of breast cancer, with more pejorative criteria compared to non-inflammatory breast cancer: younger age, negative ER, positive HER2, High SBR grade, lymph nodes and metastatic diffusion. This is explaining the poor prognosis of this disease.

Maximal result can be performed by multimodal treatment (neoadjuvant chemotherapy + surgery + adjuvant irradiation +/− adjuvant chemotherapy) for localized disease.

Other active treatments must be studied and validated in the future.

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Relevance of Primary Systemic Chemotherapy in &;ldquo;Luminal A" Breast Cancer

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Background: Since the concept of intrinsic subtypes based on gene profiles was introduced, treatment strategies for breast cancer have changed. However, patients and doctors often encounter difficulties choosing appropriate treatments because of uncertain subtype definitions. Luminal A (LumA) tumours are good targets for endocrine therapy while responses to chemotherapy are poor. Thus, there is now controversy as to whether to give primary systemic chemotherapy (PSC) to LumA patients. We investigated the effect of PSC in LumA to identify factors possibly predicting a good response to this treatment.

Methods and Patients: We studied 220 patients who received PSC during the 2006 through 2008 period at our institution. These patients were given CEF (epirubicin: 75–100 mg/m^2, 4 cycles) followed by taxane (paclitaxel: 80 mg/m^2, weekly, 12 treatments; or docetaxel: 75 mg/m^2, tri-weekly, 4 cycles). Chemotherapeutic effects were determined by pathologists using the General Rules for Clinical and Pathological Recording of Breast Cancer of the Japanese Breast Cancer Society. Among Her2 negative luminal tumours, we judged disease to be luminal B (LumB) if tumour grade or the Ki67 index (>30%) was high. Eighty-seven LumA tumours, among 220, were specifically examined for tumour characteristics and biomarkers. We also evaluated the expressions of proteins regulating tumour proliferation, such as FOXM1, by immunohistochemistry (IHC).

Results: As to the subtype proportions; LumA: 40%, LumB: 19%, Her2: 24%, triple negative: 18%. The overall pCR rate was 17%. The pCR rate in LumA was only **7%** while LumB, Her2 and triple negative tumours had rates of 13, 29 and 23%, respectively. We found no specific difference between pCR and non-pCR among LumA cases in age, tumour structure, grade, ER, or PR. However, when two LumA groups, good and poor responders to PSC, were compared, there were significantly more PR-negative tumours among those showing good responses. The 46% of LumA that are PR-negative constitute a good response group while only 25% of PR-positive LumA responded to chemotherapy. As for IHC results, LumA with low FOXM1 expression showed a better response to PSC.

Conclusion: PR-negative tumours had better responses to PSC. Further investigations are needed to reveal which LumA patients are likely to benefit from PSC, which would increase possibilities for breast conserving surgery.

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Primary Systemic Therapy for Hormone-sensitive Breast Cancer − in View of Ki-67 Labeling Index

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Background: Chemotherapy effect for hormone-sensitive breast cancer is controvertible, while high proliferation as measured by Ki-67 is one of the factors arguing for the inclusion of chemotherapy. We reviewed results of primary systemic therapy (PST) for our hormone-sensitive breast cancer patients to examine the correlation between PST effect and Ki-67 labeling index.

Material and Methods: Among 117 primary breast cancer patients, who underwent PST in our hospital between 2009–2011, We studied with 61cases, which were hormone receptor positive (ER⩾10% andPgR⩾10%) and negative Her2 status. We classified them into 3 groups; Ki-67 low (<15%), moderate (⩾15%, <30%), and high (⩾30%), and reviewed their PST effect categorically.

Results: 35 patients received neoadjuvant chemotherapy while 26 patients underwent neoadjuvant endocrine therapy. Clinical response rate for neoadjuvant chemotherapy group was; Ki-67 low: 87.5% (7/8), moderate: 81.8% (9/11), high: 93.7% (15/16). 3 cases with high Ki-67 achieved pathological complete response, but no cases with low or moderate Ki-67. In neoadjuvant endocrine therapy group, on the other hand, clinical response rate was; Ki-67 low: 36.4% (4/11), moderate: 62.5% (5/8), high; 14.3% (1/7). 1 case with moderate Ki-67 and 1 case with high Ki-67 developed progressive disease. Pathological complete response was achieved in only 1 case with low Ki-67.

Conclusions: Our results indicate that hormone-sensitive breast cancer with high Ki-67 tends to be more responsive to chemotherapy, but less to endocrine therapy, which may support St. Gallen Consensus 2011; neoadjuvant chemotherapy is less useful in the Luminal A subtype, while is considered for Luminal B disease.