consevutively or 6 cycles of AD and then complete resection. Each cycle of chemotherapy in this group was performed at the interval of 3 weeks. The group of ACT was scheduled for 4 cycles of AC regimen (50 mg/m^2 and 500 mg/m^2, respectively) and then 4 cycles of paclitaxel(175 mg/m^2) at the interval of 3 week, respectively, before surgery. The patients who were confirmed systemic metastasis at the time of initial diagnosis or within 3 month after surgery and received therapy other than routine scheduled regimen were excluded.

Results: The patients who were enrolled in this study were totally 78 (AD and ACT were identically 38.) The significant differences of patients' characteristics before neoadjuvant chemotherapy were not observed between two groups. However, the significant differences were identified in hematologic toxicity including neutropenia more than grade 3 ($p < 0.001$), neutropenic fever ($p < 0.001$), dose reduction due to hematologic toxicity ($p = 0.012$) and chemotherapy induced anemia ($p = 0.012$), although chemotherapy induced thrombocytopenia ($p = 1.0$) was not different between two gruops. No differences were identified in non-hematologic toxicity including hepatic toxicity [AST ($p = 1.0$), ALT ($P = 0.783$) and bilirubin($p = 1.0$)], gastrointestinal toxicity [nausea, vomiting ($p = 0.529$) and diarrhea ($p = 1.0$)[and peripheral neuropathy ($p = 1.0$). The response of chemotherapy was no difference between two group, which was estimated by conversion rate of breast conserving surgery ($p = 1.0$), clinical response of chemotherapy ($p = 0.148$), clinically downstaging rate ($p = 0.464$) and pathologic complete response rate ($p = 1.0$). There is no factor to predicting pathologic complete response or conversion to breast conservation in this study.

Conclusions: The ACT regimen, compared to AD regimen, has an equivalent response to chemotherapy and a less side effect.

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Recurrence Score (RS) and Treatment Decisions in Node-positive (N+), Estrogen Receptor-positive (ER+) Breast Cancer Patients in Israel

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Background: RS, determined using the Onco*type* DX® assay, has a prognostic utility and can predict response to chemotherapy in node negative ER+ breast cancer patients. We evaluated the relationship between RS and treatment decisions in N+/ER+ breast cancer patients in Israel.

Materials and Methods: Eligible patients had micrometastases (Nmic) or 1−3 positive nodes, ER+ breast cancer and were reimbursed by Clalit Health Services (CHS) for the Onco*type* DX assay between 3/2006 and 11/2009. Claims data were reviewed to identify treatment received (chemotherapy plus hormonal therapy [CHT] vs hormonal therapy alone [HT]).

Table: Proportion of CHT-treated patients by RS, nodal status, and age group

Age group	Low RS (<18)	Intermediate RS (18−30)	High RS (⩾31)
Nmic			
<40 y (n = 3)	0% (0/1)	− (0/0)	100% (2/2)
40−55 y (n = 51)	3.6% (1/28)	26.3% (5/19)	100% (4/4)
>55 y (n = 81)	4.1% (2/49)	28.0% (7/25)	100% (7/7)
Total (n = 35)	3.8% (3/78)	27.3% (12/44)	100% (13/13)
1 positive node			
<40 y (n = 2)	0% (0/1)	100% (1/1)	− (0/0)
40−55 y (n = 27)	26.7% (4/15)	63.6% (7/11)	100% (1/1)
>55 y (n = 72)	7.1% (3/42)	35.7% (10/28)	100% (2/2)
Total (n = 101)	12.1% (7/58)	45% (18/40)	100% (3/3)
2−3 positive nodes			
<40 y (n = 1)	− (0/0)	0% (0/1)	− (0/0)
40−55 y (n = 10)	0% (0/6)	50% (2/4)	− (0/0)
>55 y (n = 35)	7.1% (1/14)	42.1% (8/19)	100% (2/2)
Total (n = 46)	5.0% (1/20)	41.7% (10/24)	100% (2/2)
All patients			
N = 282	7.1% (11/156)	37.0% (40/108)	100% (18/18)

Results: 282 patients were included in the analysis (6 patients <40 y; 88 patients between 40 and 55 y; 188 patients >55 y). Distribution of nodal status and age as well as RS results are shown in the Table. In total, after having the RS, 69 patients (24%) received CHT and 213 patients (76%) received HT. Overall, 7% of patients with low RS, 37% of patients with intermediate RS, and 100% of patients with high RS received CHT. In all examined nodal status groups, the proportion of CHT-treated patients was smaller in the low RS group than in the corresponding intermediate RS group and all patients with high RS received CHT (Table).

Conclusions: The RS seems to impact treatment decisions in N+ (Nmic or 1−3 positive nodes) ER+ breast cancer patients over 55 y in Israel more than nodal status. In younger patients data are limited due to a small sample size.

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Phase II Study of Neoadjuvant Pegylated Liposomal Doxorubicin and Cyclophosphamide +/− Trastuzumab Followed by Docetaxel in Locally Advanced Breast Cancer (LABC)

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Background: The primary end point of this study was the clinical response rate of neoadjuvant pegylated liposomal doxorubicin (Caelyx®) and cyclophosphamide +/− trastuzumab followed by docetaxel in patients with LABC. Secondary end points included determination of the rate of pathological complete response (pCR) and evaluation of the safety of the combination regimen.

Material and Methods: Patients (pts) with inflammatory, locally advanced breast cancer or a tumor >5 cm were enrolled. Pts received 4 cycles of pegylated liposomal doxorubicin 35 mg/m^2 and cyclophosphamide 600 mg/m^2 on q21d followed by 4 cycles docetaxel 100 mg/m^2 q21d. Pts with HER2-positive tumors were concurrently treated with trastuzumab 6 mg/kg q21d for 8 cycles.

Results: From March 2009 to October 2010 49 pts were enrolled. One pt was excluded from the study as she turned out to have sarcoma. Thus, 48 pts were assessable for toxicity. The median age was 50 years (range 31−69). 26 pts. (54%) were premenopausal and 22 (46%) postmenopausal. 14 pts (29%) had tumor T4, 32 (67%) T3 and 2 (4%) T2. 11 pts (23%) had HER2-positive tumor and 7 (15%) had triple negative tumor.

All 8 cycles of neoadjuvant therapy were completed as planned in 40 pts (83%), 6 (13%) discontinued treatment due to toxicity after 5−7 cycles and 2 pts discontinued due to clinical suspicion of progression and patient's wish, respectively. One patient developed an anaphylactic reaction to the first infusion of pegylated liposomal doxorubicin. 47 pts were therefore assessable for response evaluation.

Investigator-assessed clinical response rate was 83%, 3 pts (6%) had a clinical complete response and 36 (77%) had a partial response. One patient was clinically suspected for progression but operation showed response. pCR rate was 19% (9 pts).

The primary toxicity observed was skin toxicity. Palmar-plantar erythrodysesthesia (PPE) grade 3 was observed in 10 pts (21%) and grade 4 in 6 (13%). Other most frequent grade ⩾3 adverse events were: pain (31%), neurotoxicity (21%), fatigue (21%), febrile neutropenia (19%), mucositis (8%). No changes in cardiac function were seen. There were no treatment-related deaths.

Conclusions: The combination of pegylated liposomal doxorubicin and cyclophosphamide +/− trastuzumab followed by docetaxel is highly active in LABC with an acceptable safety profile. The primary toxicity was cutaneous toxicity which was manageable.

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Genetic Variability in the Methylenetetrahydrofolate Reductase (NAD(P)H) Gene (MTHFR) is Associated with Severe Non Hematological Toxicity of Adjuvant FEC in Breast Cancer

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Background: We assessed the impact on non hematological chemotherapy toxicity of single nucleotide polymorphisms (SNP) in germline DNA in a panel of potential genes of interest through high throughput sequencing. First aim was to validate the predictive value of certain SNP

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.