radiotherapy – 152 (73%); disease status – AWOD – 164 (82%), DWD – 31 (15%), AWD – 6 (3%).
The only statistically-significant prognostic parameters for OS on CPHM were tumor size ($p < 0.001$), lymph-node-status ($p < 0.001$), location ($p < 0.001$), and grade ($p = 0.007$), and for PFS were tumor size ($p < 0.001$), location ($p = 0.01$), and lymph-node-status ($p = 0.03$). The only statistically-significant prognostic parameters for OS on LGM were menopausal status ($p < 0.001$), grade ($p < 0.001$), and progesterone-receptor status ($p < 0.001$), and for PFS was tumor size ($p < 0.001$).
Conclusions: This retrospective, single-institution experience validates: a) the prognostic importance of classic clinicopathological parameters including the stats of menopause, tumor size and location, lymph-node, grade and progesterone-receptor, and b) The limited prognostic value of various immunohistochemical parameters commonly-used in practice.

5153 POSTER

The influence of polymorphism in TYMS, MTHFR and GSTP1 genes on toxicity and response in breast cancer patients treated with adjuvant chemotherapy

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Background: Genetic polymorphism in drug-metabolising enzymes and drug targets are known to be responsible for inter-individual differences in cancer treatment response and toxicity of various types of chemotherapeutics. *TYMS* and *MTHFR* variants may affect 5-fluorouracil (5-FU), capecitabine and methotrexate metabolism, while *GSTP1* influences detoxification of cyclophosphamide, doxorubicin, etoposide and platinum compounds. In the present study, 28-bp tandem repeat in *TYMS* promoter (TSER), *MTHFR* Ala222Val and *GSTP1* Ile105Val polymorphisms were investigated in relation to adverse effects in 135 breast cancer patients receiving neoadjuvant (4−9 cycles) and adjuvant (4−6 cycles) chemotherapy based on 5-FU, i.e. CAF, CMF, (n = 100) or AC, AT, TAC (n = 35) regimens.
Material and Methods: There were 135 women (mean age: 54 years, range 27−78) diagnosed with breast cancer stage I-IV included in the study. Ductal carcinoma accounted for the most frequent type of cancer (65%). Physical examination and full blood count were performed before each chemotherapy cycle. Toxicity was recorded according to the WHO criteria, after each cycle. The assessment of response concerned patients receiving neoadjuvant chemotherapy. It was based on physical examination, magnetic resonance and histopatological examination of tumor and lymph nodes of axilla. DNA was isolated from peripheral blood and the genotypes were identified using standard PCR-RFLP assay.
Results: Overall toxicity grade 3−4 was observed in 20% of patients. There were more *TYMS* 3R/3R carriers among cases with overall toxicity grade higher than 2 in all group ($P = 0.016$) and in patients receiving 5-FU-based therapy ($P = 0.047$). Also hematotoxicity grade 2−4 was noticed more often among 3R/3R homozygotes ($P = 0.076$). When gastrointestinal toxicity has been considered, grade > 2 was observed exclusively in *GSTP1* Ile/Ile or Ile/Val carriers in 5-FU treated subgroup ($P = 0.020$). Nausea and vomiting grade 2−3 were also associated with *GSTP1* Ile allele ($P = 0.058$). Response rate (complete or partial) in the group was 42%. There was slight preponderance of *TYMS* 3R/3R homozygotes and heterozygotes among responders *versus* nonresponders ($P = 0.077$). In treated with 5-FU in turn, 2R allele was found to be prevalent among good responders ($P = 0.051$).
Conclusions: Our preliminary results show that polymorphisms in *TYMS* and *GSTP1* may serve as useful predictors of toxicity and efficacy of chemotherapy in breast cancer patients, however large-scale, prospective studies are warranted.

5154 POSTER

Triple-negative high grade invasive ductal breast carcinomas are biologically heterogeneous: differences between the basal and non-basal subtypes

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Background: Triple-negative breast carcinomas (TNBC) are characterized by their unique molecular profile, aggressive behavior, distinct patterns of metastasis, and lack of targeted therapies. Although not synonymous, the majority of triple-negative breast cancers carry the “basal-like” molecular profile on gene expression arrays. Our objective was to explore the clinicopathological characteristics of TNBC.
Material and Methods: We selected 31 consecutive cases of invasive ductal carcinomas, histological grade 3, negative for estrogen and progesterone receptors (ER/PR) and HER2 protein. We examined differences between the basal subtype determined by expression of basal cytokeratins and/or epidermal growth factor receptor, and the non-basal phenotype in relation to age, tumor size, axilla involvement, presence of lymphvascular embolization and immunoexpression of p-cadherin and p53.
Results: The results are summarized in table 1.

Table 1: Differences between the basal and non-basal subtypes of triple negative breast carcinomas of histological grade 3

subtype	n	Age range (median)	Tumor size range (median)	LVE positive (%)	Axilla positive (%)	p-cadherin (%)	p53
basal	23	30−94 y (46)	2−16 cm (4.0 cm)	8 (34.8%)	12/18 (66.7%)	4 (17.4%)	16 (69.5%)
Non-basal	8	43−66 y (51)	2−10 cm (5.3 cm)	1 (12.5%)	4/7 (57.1%)	2 (25%)	5 (62.5%)

LVE = lymphvascular embolization.

Conclusions: TNBC of the basal subtype occur in younger patients and show more aggressive pathological characteristics compared to non-basal subtype, confirming the heterogeneity of the group.

5155 POSTER

Time-dependence of hazard ratios for prognostic factors in patients with early breast cancer

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Background: After surgical treatment of early breast cancer a life long risk for relapse persists. Hazard ratios for relapse can change during the follow-up period. The aim of our study was to study time-dependence for classical prognostic factors for relapse (age, tumor stage and grade, histological type, estrogen receptors, lymphovascular invasion (LVI) and of axillary lymph nodes involvement).
Materials and Methods: In 1035 patients with early breast cancer treated between 1983−87 at the Institute of Oncology Ljubljana (median follow-up was 17 years) we retrospectively analysed prognostic factors for relapse with Cox proportional hazard model and with test for violation of proportional hazard assumption (method of Schoenfeld’s residuals).
Results: Tumor size, grade and estrogen receptors (ER) were time-dependent prognostic factors for breast cancer relapse. Tumor size >2 vs. $\leqslant$2 cm (HR 1.59; 95% CI 1.21−2.10) and grade G2/3 vs. G1 (HR 2.08; 95% CI 1.39−3.13) were unfavorable prognostic factors in the first five years after surgery and lost their prognostic role thereafter. Positive ER (ER+ vs. ER) were a favorable prognostic factor only in the first year after surgery, from 1−5 years they had no prognostic role, after 5 years they became borderline unfavorable prognostic factor (HR 1.50 95% CI 0.98−2.30). Positive axillary lymph nodes (4−9 lymph nodes: HR 2.55; 95% CI 1.91−3.40; $\geqslant$10 lymph nodes: HR 4.65; 95% CI 3.29−6.58) and LVI (HR 1.58; 95% CI 1.21−2.06) were time-independent risk factors throughout the follow-up.
Conclusions: Tumor stage and grade are time-dependent unfavorable prognostic factors, being significant only in the first 5 years after surgery. Positive ER changes their prognostic role with time, from being shortly favorable to being unfavorable. More then 3 involved axillary lymph nodes and LVI are time-independent unfavorable prognostic factors throughout the follow-up period.

5156 POSTER

A tool to improve personalized cancer care: measuring the response of circulating epithelial tumour cells (CETC) and tumour stem cell subpopulations to therapy in the individual patient

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Background: Cells released from the primary tumour persisting and recirculating in the host can lead to the formation of distant metastases. We can show that CETC are detectable and can be quantified in the peripheral blood of almost all cancer patients including early-stage solid malignancies, although it was claimed that such cells are detectable only in a minor fraction of early-stage cancer patients.
Material and Methods: Using anticoagulated peripheral blood and red blood cell lysis as the only enrichment step, one centrifugation step, staining live cells with fluorochrome labelled anti-epithelial antigen as a search antibody, automated image analysis for detection of positive events