A). No correlation (p = NS) was found between hormone receptors and CEA, CA 15−3, and MIB-1 in both groups.

Conclusions: Our results suggests that (1) baseline STM CEA and CA 15−3 are not useful for prognostic purposes, (2) age, size, and ER are week isolated prognostic factors, and (3) the cumulative risk of relapse increases in the presence of multiple factors such younger age associated with highest levels of STMs and MIB-1, and low ER rate, together.

References

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329 Poster

Expression of MMTV-homologous Sequences in the Patients with Breast Hyperplasia and Ductal Carcinoma in Situ

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Background: Earlier, mouse mammary tumor virus (MMTV)-related sequences were revealed in significant proportion of human breast cancer (BC) tissues and blood sera samples. Mammary hyperplasia (MH) and ductal carcinoma in situ (DCS) are considered as a first steps for BC progression. A relationship between expression of MMTV-related provirus (hMTV) genome sequences and BC initiation/ progression is mostly unclear.

Material and Methods: 25 DCS and 10MH fresh or fixed archival tissues and blood samples from 35 primary patients (age is 21−56 years old) were studied by PCR and one-tube RT PCR after DNAase treatment to avoid pseudo positive results. Tumor histology was verified by routine staining of BC or normal tissue sections. Specific PCR products were sequenced and compared by BLAST and/or CLUSTAL programs.

Results: DNA sequences with 92%-95% homology to the *env* MMTV gene and 89−97% homology to 3′LTR MMTV were revealed in 11/25 (44%) DCS and 3/10 (30%) MH tissue samples, as well as in 17/25 (68%), 5/10 (50%) blood samples, correspondingly, *vs* 0/7 normal mammary tissue control samples. All hMTV-positive patients, except five ones, had pathological immune system status: rheumatoid arthritis, chronic lung infections, dental or nosofaringeal diseases. The hMTV sequence expression was found in 9/25 DCS and 3/10 H tissue samples. The sequences integration sites were studied by RACE method and were sporadic, without any predominant genome localization. An analysis of more number of malignant mammary tissue samples would clear provirus integration pattern and its possible localization near cell oncogenes.

Conclusions: a preliminary data suppose a role of hMTV sequences expression as a risk factor for genome instability and MH or DCS development. Cloning and sequencing of *env, gag*, Sag and HRE-coding hMTV sequences revealed in DCS and MH samples and its prognostic evaluation is in process.

330 Poster

Leptin and VEGFR Expression in Sporadic Breast Cancer Patients

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Background: Hormone leptin (Lep) is produced by adipose tissue and regulates cell metabolism and growth through signal transduction by interaction with leptin receptor (LepR). It is found that LepR-dependent signal pathways have common points with VEGF-dependent ones. Lep signaling regulates VEGF activity mainly through HIF-1α and NFkappaB. The effects of Lep/LepR expression on mammary cell proliferation and proteins associated with Lep /LepR signaling are important for understanding of breast cancer (BC) induction and progression, especially in BC patients suffered with obesity and other metabolic diseases.

Material and Methods: Expression of Lep/LepR and VEGFR-2 was studied in tumor tissues samples obtained from 15 sporadic BC patients (4 − obesity, 3 − high body mass, 8 − normal body mass, 24−45 yo, mean age 32$\pm$6.4 yo) using immunohistochemistry and RT PCR. Tumor and normal mammary tissue images (100–150 per sample) obtained by using monoclonal antibodies anti-LepR, anti-VEGFR-2 (Dako) and immunohistochemical staining (EnVision system, Dako) were analysed by MatLab 7.0 program. The data were compared with RT PCR results obtained by using total tumor RNA as a matrix and specific primers for *Lep, LepR* long isoform and *VEGFR-2* gene regions.

Results: Mean density of stained anti-LepR granules was significantly higher in tumor mammary tissues than in normal tissue: LepR − 37.4$\pm$3.6 *vs* 8.2$\pm$2.3, $p < 0.002$; mean density of anti-VEGFR-2 granules per length unit of vascular endothelium was 1.78$\pm$0.62 *vs* 0.82$\pm$0.34, $p < 0.05$. RT PCR results confirms that Lep, LepR and VEGFR-2 expression levels in BC tumors under study were significantly higher in tumor mammary tissue than in normal mammary tissue of sporadic BC patients. Moreover, LepR expression correlated with Lep and VEGFR-2 expression. There were no any relationships between body mass index and Lep/LepR/VEGFR-2 expression levels, probably, because of small patient number.

Conclusions: The results confirm high expression level of Lep/LepR/VEGFR-2 in mammary tumor cells in sporadic BC patients. A concordance between high LepR − Lep and LepR/Lep − VEGFR-2 expression levels in BC tissues in spite of patient body mass was also revealed. The data supports an involvement of Lep/LepR signalling into mammary tumor carcinogenesis; it is indicative of Lep regulation of VEGF/VEGFR expression. Continued study of prognostic value for Lep/LepR expression using results of immunohistochemistry, ELISA and RT PCR is in process.

331 Poster

What is the Influence of Early Loco-regional Recurrence in Triple-negative Breast Cancer Patients on Disease Outcome?

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Introduction: Triple negative breast cancer (TNBC) is a biologically heterogeneous group of breast tumors with generally poor prognosis. The aim of this analysis was to investigate how early occurrence of loco-regional relapse (LRR) influenced the outcome of these patients (pts).

Patients and Methods: From June 2006 to the end of 2009 a total of 243 stage I-IIIB TNBC pts were diagnosed at the Institute for Oncology and Radiology of Serbia. Since 21 pts were lost to follow up, 222 pts were analyzed. TN status was defined as IHC ER0−3/PR0−3/HER2:0−1 or IHC HER2:2+/CISH−. The majority of them had radical surgery +/− postoperative radiotherapy (RT) and adjuvant chemotherapy (CHT) as per protocol. The main end points were disease-free survival (DFS) defined as the time between surgery and BC relapse or death without BC relapse, and overall survival (OS) defined as the time from BC diagnosis to death from any reason. Statistics included Pearson Chi-squared test and Log-rank test.

Results: During the median follow up period of 25 months (range 3−58) LRR occurred in 15/222 (7%) pts, 5 of whom developed synchronous distant metastases. At the same time 28/222 (13%) pts were diagnosed with distant relapse only. Significantly higher proportion of LRR pts are older than 65 years (60%) and had positive nodal status (67%) compared to pts without LRR (27% and 36%, respectively) (c_1^2 test, p = 0.019 and c_1^2 test, p = 0.006, respectively). We looked separately at a group of pts with LRR only (10/222) and compared their disease outcome with pts who developed distant metastases. There was no significant difference in DFS [15 ms (95% CI 4.2–25.8 vs. 13 ms (95% CI 7.8–18.2)] and OS [39 ms (95% CI 10.0–67.9) vs. 40 ms (95% CI 33.6–46.4)] between LRR only and distant metastasis groups of pts (Log rank test, p > 0.05 for both).

Conclusion: Our results seem to point out that early relapse in TNBC pts means decreased survival irrespective of the first relapse site (loco-regional only vs. distant metastases).

332 Poster

Evaluation of Molecular Parameters and Risk Factors of Breast Cancer in Therapeutic Decisions

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Introduction: Biological characteristics of breast cancer (BC) are of increased importance in treatment decision. Molecular parameters (MP) considered of prognostic importance can be positively correlated with more traditional risk factors (RF) or might change an initial prognosis based on these RF. We purposed to review our clinical practice using data of patients admitted in our institution with BC from 1.Jan.2007 until 31.Dec.2007 and identify the association between MP and RF and how this affected treatment decision and survival.

Methods: Demographic and clinical characteristics of patients were reviewed using clinical records. As RF considered in treatment options we considered: age (<35 years old and >35 years old) and TNM stage. The MP investigated were: grade (G), hormonal receptors (HR), HER2. An indication for chemotherapy was used as surrogate of clinical consideration of worse prognosis. Statistical package SPSSv.17 was used for statistic analysis and categorical variables were compared using x^2 test and continuous variables using Mann-Whitney U test. A p value <0.005 was considered of statistically significance. A multivariate analysis using