outcome compared to pts with some expression of ER (Allred score 2–3) and PR (Allred score 2–3) and HER2 (IHC 1+ and IHC 2+/CISH−) (non-TN0 subgroup).

Methods: From 2006, until 2010, 594/4912 (10%) newly diagnosed TNBC pts were identified. We analyzed 165/594 (36%) pts who were operated on from resectable BC (stage 1–3) and treated with postoperative radiotherapy and adjuvant systemic therapy as per protocol. IHC was used for ER, PR and HER2 determination, and CISH analysis was done for IHC HER2: 2+ BCs. The whole group was divided into two subgroups: TN0 and non-TN0. Disease free survival (DFS) and overall survival (OS) were the main end points. Fisher Exact Test, Pearson Chi-squared Test, and Log-rank test were used for statistical analysis.

Results: A total of 165 pts median age of 58 years (range 26–84), were equally divided according to SR and HER2 expression: 83 pts inTN0 and 82 pts in non-TN0 subgroups. Subgroups were homogenous according to the age, menopausal status, clinical stage at diagnosis, tumor size and grade, nodal status, type of surgery, postoperative radiotherapy and adjuvant chemotherapy regimen administered. Adjuvant endocrine therapy was administered in significantly higher number of pts in non-TN0 subgroup (Fischer Exact test, $p = 0.0087$). After median follow up of 26 months (range 2–55) disease relapse experienced 10.9% of pts, while 2.4% pts died. There were no difference in DFI (Log-rank test; $\chi^2_1 = 2.001$, $p = 0.157$) and OS (Log-rank test; $\chi^2_1 = 1.197$, $p = 0.274$), and in 1-year, 2-year and 3-year cumulative incidence in disease relapse and deaths between the two subgroups, as well. We also looked at ER0/PR0 group regardless of HER2 expression and found that 83.6% pts were ER0/PR0, while only 13.9% had some expression of ER/PR. There was a trend of higher association of ER0/PR0 tumors with medullar histology, grade 3 tumors and adjuvant CMF therapy. There were no differences in time to events between these two subgroups during the same follow-up period.

Conclusion: Although obtained on a small number of pts, our results showed that after short follow-up period one tenth of TNBC pts experienced disease relapse. Pts with poorer prognosis in TNBC group could not be discriminated by lack of expression of either ER/PR or ER/PR/HER2.

Disclosure of Interest: None Declared

P189 The methylation status of estrogen receptor-α negative [(ERα(−)] in correlation with the methylation status of SOCS1 gene in primary breast carcinoma (BC)

K. Desiris[1], S. Voyatzi[1], M. Markopoulos[1], A. Kiziridou[1], P. Stravoravdi[1], G. Simpilidis[1]. [1]*Research, Theageneio Cancer Hospital, Thessaloniki, Greece*

Goals: DNA hypermethylation of CpG islands in promoter region of a gene is an epigenetic mechanism of gene regulation. ER status of breast cancer is clinically important, and is used both as a prognostic indicator and treatment predictor. SOCS1 (Suppressor of Cytokine Signaling) gene plays an essential role in cytokine-mediate processes, suggesting a role in the suppression of carcinogenesis. The objective of the present study was to determine whether ERα(−) methylation status relates to epigenetic changes in SOCS1 gene.

Methods: A panel of 50 female patients (pts) with primary BC of known ERα status (40/50 ERα-negative; 10/50 ERα-positive) was studied. Genomic DNA was extracted from archive formalin-fixed paraffin-embedded tumor tissues. DNA methylation for ERα and SOCS1 was determined by chemical modification of DNA and subsequent double "hot start" Methylation-Specific PCR (MSP), followed by detection on agarose gel. The immunohistochemical expression of HER2 protein was studied according to the ASCO-CAP guidelines.

Results: Methylation of ERα(−) gene was observed in 13/40 pts (32.5%). Correlation of these cases with PR status and HER2 protein expression revealed that 13/13 pts demonstrated PR-negative and 10/13 HER2-negative protein expression; 10/13 pts were triple-negative. The ERα(−) methylation status was not correlated with age, tumor size, grade and lymph node metastases. None of these 13 pts presented methylation of SOCS1 gene. The SOCS1 CpG islands were hypermethylated in only 1/27 ERα(−) patient who did not present methylation in ERα(−) gene. This patient had PR negative and HER2 positive protein expression. In ERα(+) BC pts methylation did not occur either in ERα or SOCS1 gene.

Conclusion: Our results suggest that no correlation exist between the methylation status of ERα(−) and SOCS1 genes. Also, SOCS1 gene is rarely hypermethylated in primary BC. So, the contribution of silencing or inactivation of SOCS1 gene, via hypermethylation, in breast carcinogenesis seems to be of lesser extent compared with other solid tumors.

Disclosure of Interest: None Declared

P190 Molecular breast cancer subtypes: relationship with clinicopathological characteristics, efficacy of neoadjuvant chemotherapy and survival

N. Babyshkina[1], E. Malinovskaya[1], M. Zavyalova[2], N. Cherdyntseva[1], E. Slonimskaya[3]. [1]*Department of Experimental Oncology, Cancer Research Institute,* [2]*Siberian State Medical University,* [3]*Department of General Oncology, Cancer Research Institute, Tomsk, Russian Federation*

Goals: Recent studies have emphasized the importance of the molecular portraits of breast cancer for use of new treatment strategies and prognostication of disease. The aim of this study was to evaluate the clinicopathological characteristics, the response to treatment and clinical outcomes of breast cancer patients according to molecular cancer subtype.

Methods: A retrospective analysis was performed for 304 Russian breast cancer patients of Western Siberian region selected on the basis of neoadjuvant chemotherapy and the availability of immunohistochemical data for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER-2/neu) status.

Results: There were significant differences in the ages at diagnosis by breast cancer subtype; the median age for triple negative (TN) cases was 49.5 years, while for luminal A and HER2+ median ages were 53.1 and 52.4 years, respectively ($P = 0.04$). Women with HER2+ subtype had significantly larger primary tumor size as compared with luminal A ($P = 0.0001$) and TN ($P = 0.01$) patients. TN subtype tended to show an association with stromal inflammatory infiltration than luminal A ($P = 0.06$). We found that the patients with triple negative disease had a significantly better clinical response to neoadjuvant chemotherapy compared to luminal A cases ($P = 0.02$). Nonetheless, TN patients had shorter overall survival, by log-rank analysis than HER2+ patients, although the differences did not reach statistical significance ($P = 0.059$).

Conclusion: These findings indicate that triple-negative subtype is associated with younger patient age, a comparable response rate to neoadjuvant chemotherapy and poorer outcome in terms of overall survival. In the future, with the additional characterization of all molecular subtypes, personalized treatment strategies could be developed to increase the chemotherapeutic efficacy and survival of breast cancer patients.

Disclosure of Interest: None Declared

P191 Macrocytosis predicts response to metronomic chemotherapy with capecitabine and cyclophosphamide in combination with bevacizumab

S. Dellapasqua[1], V. Bagnardi[2], F. Bertolini[3], M.T. Sandri[4], D. Pastrello[1], G. Cancello[1], E. Montagna[1], A. Goldhirsch[5], M. Colleoni[1]. [1]*Medical Senology Research Unit – Dept. of Medicine,* [2]*Division of Epidemiology and Biostatistics,* [3]*Division of Hematology-Oncology,* [4]*Unit of Laboratory Medicine,* [5]*Division of Medical Oncology, Istituto Europeo Di Oncologia, Milano, Italy*

Goals: There is an urgent need for the identification of commonly assessable predictive factors in the treatment of patients with metastatic breast cancer.

Methods: During the course of a treatment which included low dose metronomic oral cyclophosphamide (Endoxan®, Baxter, 50 mg daily) and capecitabine (Xeloda®, Roche, 500 mg 1 tablet thrice daily) plus i.v. bevacizumab (Avastin®, Roche, 10 mg/kg i.v. every 14 days or 15 mg/kg i.v. every 21 days) we observed that a relevant number of metastatic breast cancer patients developed macrocytosis [MCV (mean corpuscular volume) $\geqslant$100 fl] without a significant fall in hemoglobin levels. We conducted a retrospective analysis on these 69 patients to evaluate if macrocytosis was associated to tumor response.

Results: MCV increased significantly ($p < 0.001$), with 42 out of 69 patients (61%) developing macrocytosis during the course of treatment, while hemoglobin levels remained stable ($p = 0.27$). Using Cox proportional hazards modeling that incorporated macrocytosis as a time-dependent covariate, macrocytosis resulted in a halved risk of disease progression (HR 0.45; 95% CI, 0.22–0.92, p-value 0.028). In a landmark analysis limited to patients with no sign of progression after 24 weeks of treatment, median