Treatment outcomes in triple negative breast cancer patients undergoing neoadjuvant chemotherapy. The importance of Ki-67.

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Introduction: The aim of this retrospective project is to evaluate the treatment outcomes including; pathological complete response (pCR), time to progression and overall survival in triple-negative breast cancer (TNBC) patients (pts) treated with taxane, and/or anthracycline/alkylating agents based neoadjuvant chemotherapy.

Background: Ki-67 immunohistochemical determination is a widely used biomarker of cell proliferation in pts undergoing endocrine treatment for breast cancer. The role of Ki-67 in TNBC pts undergoing NAC for early disease remains controversial.

Methods: The study retrospectively analyzed clinical and pathological data on 86 patients (pts) with TNBC. Pathological complete response (pCR) was defined as the complete disappearance of the invasive cancer in the breast and absence of tumor in the axillary lymph nodes examined by axillary clearance. The purpose of this analysis was to investigate factors associated with pCR and time to progression. Demographics, patient characteristics, Ki-67 and molecular subtype were analyzed using descriptive statistics, chi-square and T-tests receiver-operating characteristic (ROC) curve analysis was used to determine the optimal cut-off points for Ki-67. Univariate analysis (logrank test) was used to determine the effect of pCR on time to progression of these pts. A logistic regression analysis was used to determine the effects of each variable on pCR. Ethical approval was obtained from Pharma-Ethics before the initiation of the project.

Results: There were 35 pCR's (40.7%; 95% CI 33.4%-55.3%). At 2 years 82% of pts who attained a pCR were disease free compared to 67% of pts who did not attain a pCR (log rank test $p < 0.0117$). On univariate analysis factors associated with higher pCR included primary tumor size (T1=84% vs T2 and T3 =50% of pts, $chi^2 = 6.81$, $p<0.03317$), Ki67 (>30=68% vs. eq or < 30%= 18% of pts, $p<0.00020$), age (< than 50 =71% vs. equal or >50 =44% of pts), tumor grade (1=88% vs. 2=60% vs. 3=44% of pts, $chi^2 = 6.2560$ $p<0.04381$) and stage (I= 89% vs. IIA=60% vs. IIB=46% vs. III=40% of pts, $p<0.01350$). Factors not associated with a higher pCR included menopausal status, extra-nodal spread and lympho-vascular invasion. A logistic regression model showed Ki-67 as a continuous variable ($p<0.012577$) and age < than 50 ($p<0.03318$) retained significance; while tumor size, stage of disease and tumor grade loss significance.

Conclusion: Ki67 and age are independent prognostic factors of pCR in pts with early TNBC undergoing neoadjuvant chemotherapy.