Prognostic factors associated with pathological complete response in early breast cancer patients undergoing neoadjuvant chemotherapy. The importance of Ki-67 and molecular subtype.

BL Rapoport (1,2), J Barnard-Tidy (1), RI Van Eeden (1), T Smit (1), SJ Nayler (3,4), C Benn (5)

1. The Medical Oncology Centre of Rosebank, Johannesburg, South Africa.
2. Department of Immunology, Faculty of Health Sciences, University of Pretoria, South Africa.
3. Drs Gritzman and Thatcher Inc. Pathology Laboratory, Johannesburg, South Africa.
4. Wits Donald Gordon Medical Centre
5. The Netcare Breast Centre of Excellence, Netcare Milpark Hospital, Johannesburg, South Africa.

Aim of study: The aim of this retrospective project is to evaluate the treatment outcomes including pathological complete response (pCR), time to progression and overall survival in patients (pts) treated with taxane, and/or anthracycline/alkylating agents and trastuzumab, based neoadjuvant chemotherapy (NAC).

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

Methods: We retrospectively analyzed data on 137 pts treated at our unit. Inclusion criteria were pts undergoing taxane and/or anthracycline, trastuzumab based NAC. Luminal A was documented in 6 pts, Luminal B in 29 pts, Her-2 positive in 30 pts and triple negative breast cancers (TNBC) in 72 pts. Data collected was the pCR for every patient - 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. Ethical approval was obtained from Pharma-Ethics before the initiation of the project.

Results: The pCR rate of the entire cohort was 41.6%. At 2 years 92% of pts who attained a pCR were disease free compared to 80% of pts who did not attain a pCR (log rank test $p < 0.0147$). On univariate analysis factors associated with higher pCR included primary tumor size (T1 68% vs. T2 41% vs. T3 or T4 0%, $Chi^2=20.05$, $p<0.00017$), nodal disease (N0 49% vs. N1 39% vs. N2 8%, $p<0.02948$), ER receptor status (negative 59% vs. positive 14%, $p<0.00000$), PR receptor status (negative 53% vs. positive 17%, $p<0.00002$), molecular subtype (TNBC 53.4%, Her2=50% and Luminal A + B was 8.5%, $p<0.00002$), Ki67 (>40=55% vs. 15-39=34% vs. <15=0%, $p<0.00060$) and Stage (I= 85% vs. IIA=49% vs. IIB=36% vs. III=5%, $p<0.00006$). Factors not associated with a higher pCR included age, menopausal status, extranodal spread and lympho-vascular invasion.
In a logistic regression model Ki-67 as a continuous variable ($p<0.01203$) and molecular subtype ($p<0.02228$) retained its significance; while tumor size, stage of disease, nodal status, ER and PR loss significance.

Conclusion: Ki67 and molecular subtype (Her-2 positive disease and TNBC) are independent prognostic factors of pCR in pts with early BC undergoing NAC.