

June 11- 13, 2018
Dublin, Ireland

Miral Mohammed Mashhour, Arch Cancer Res 2018, Volume 6
DOI: 10.21767/2254-6081-C1-005

VALUE OF KI67 IN LOCALLY ADVANCED BREAST CANCER TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Introduction: Neoadjuvant chemotherapy is well established modality for treatment of large potentially operable and locally advanced breast cancer. Pathological complete response (PCR) following neoadjuvant chemotherapy, which is seen in 3-26% of patients is considered a good but not perfect predictor of survival. Primary breast carcinomas treated with neoadjuvant chemotherapy (NAT) provide an ideal model to evaluate the role of biological markers as predictive and prognostic factors. Ki67 index has been established as a prognostic marker in breast cancer.

Aim: This study was designed to investigate the impact of neoadjuvant therapy (NAT) on Ki67 expression and its relationship with chemotherapeutic response in locally advanced breast cancer (LABC).

Methodology: Patients with LABC (stage 2B or stage 3) who were entered into the prospective LABC database during 2002-2008 were included. The neoadjuvant regimen in these patients included anthracycline based chemotherapy (doxorubicin or epirubicin) and in patients with ER/PR negative tumors taxanes (paclitaxel, docetaxel). Ki67 was evaluated in cases with available tissue on preNAT core biopsy and postNAT specimens. Consecutive sections were studied by immunohistochemistry using antibodies directed against ER, PR, HER2/neu and Ki67 (SP6 1:800 Labvision). The percentage of Ki67 positive neoplastic cells (index) was determined using Ventana Image Analysis System. Association between Ki67 pre and postNAT and clinical response and biomarkers was evaluated.

Results: 149 patients were enrolled in the LABC database and 77 had tissue available for immunohistochemistry: 76 cases had

preNAT cores; 63 postNAT resection specimen and overall 62 had both pre and postNAT specimens. High Ki67 index on preNAT biopsy correlated with: Nottingham grade III ($p=0.03$); ER-ve ($p=0.0002$); PR-ve ($p=0.003$). High Ki67 index on preNAT biopsy did not correlate with: Her2/neu+ ($p=0.5$); nodal status ($p=0.19$); size ($p=0.51$) and; predictor of clinical response ($p=0.57$). High Ki67 index on postNAT specimen correlated with clinical response ($p=0.03$). Change in Ki67 index between preNAT and postNAT specimens occurred in 61/62 cases (38 decreased, 23 increased). Decreased Ki67 index was associated with ER+ status ($p=0.0059$) clinical response ($p=0.0047$) and increased Ki67 index was associated with triple negative ($p=0.037$)

Conclusion: There is a significant association between Ki67 index on preNAT specimen and features of aggressive behavior such as hormone receptor negativity and high tumour grade. This study indicates Ki67 index after neoadjuvant chemotherapy correlates with short term outcome in LABC patients. A recent study found that higher Ki67 values before NAC as well as lower values after NAC might be clinically significant for treating patients. Another study found that higher Ki67 expression after two weeks of endocrine NAT, but not at baseline was statistically significantly associated with lower recurrence-free survival.

Biography

Miral Mohammed Mashhour is a Consultant, Breast and Gynecologic Pathologist. She received fellowship from Toronto, Sunnybrook Hospital, Canada in 2011. She is a Chairman of biobank, she gave many presentations in national and international conferences and she published her articles in many well-known journals.

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