VALUE OF FOXP3 EXPRESSION IN PREDICTION OF NEOADJUVANT CHEMOTHERAPY EFFECT IN TRIPLE NEGATIVE BREAST CANCER

Thesis

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BY

Hazem Abd Elazim Sobhi Abo Ismael

M.B.B.Ch, Cairo University

Supervisors

Prof. Dr. Badawia Bayoumi Ibrahim

Professor of pathology
Faculty of Medicine - Cairo University

Assistant Prof. Dr. Samar Abdel Monem El Sheikh

Assistant Professor of pathology
Faculty of Medicine - Cairo University

Assistant Prof. Dr. Iman Loay Hussein

Assistant Professor of pathology
National Cancer Institute - Cairo University

Cairo University

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Abstract

Background: Response of breast carcinoma to neoadjuvant chemotherapy (NAC) varies regarding many factors including hormonal receptor status. Breast cancer is a heterogenousdisease with different outcomes,hencea need arisesfor new markers predicting the outcome of NAC especially for the triple negative group when estrogen, progesterone receptors and Her2/neu are negative. FOXP3 is apromising target with unclear role. **The aim of this study** was to examine the value of FOXP3expression in locally advanced triple negative breast cancer tumoral cells as well as tumor infiltrating lymphocytes (TILs) andto elucidate its relation to the extent of NAC response.**Material and Methods:**Forty fivecases of immunohistochemically confirmed to be triple negative breast carcinomawere evaluated for NAC response in both tumour and lymph nodes status according to Miller & Payne's and Sataloff's systems.FOXP3 expression in tumor as well as TILs evaluatedin the pretherapy biopsies was correlated with NAC response in breast tumor and lymph nodes as well as other clinicopathological factors.**Results:**Breast tumour cells showed FOXP3 positive cytoplasmic expression in (42%) of cases. High FOXP3 expression percentage was detected in (47%) of cases. High infiltration by FOXP3+TILs was detected in (49%) of cases. Positive FOXP3 expression was associated with negative lymph node metastasis. High FOXP3 expression percentage and high infiltration by FOXP3+TILs weresignificantly associated with complete therapy response in axillary lymph nodes.High FOXP3 expression in tumour cells was associated with high infiltration by $FOXP3^{+}$TILs.**Conclusion:**This result may provide evidence that FOXP3 marker is a good prognostic and predictive marker for TNBC indicated for neoadjuvant chemotherapy and

can be used for stratifications of TNBC cases indicated for NAC.As well, this study confirmed the fact that the tumour cells and the surrounding microenvironment interact with each other and the tumour microenvironment can influence the treatment outcomes of TNBC.

Key Words: FOXP3, breast cancer, Triple negative, neoadjuvant chemotherapy.

الكلمات الدالة: فوكس بى 3، سرطان الثدى، ثلاثى السلبية، العلاج القبل الجراحى

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LIST OF ABBREVIATIONS

- **ADH:** Atypical ductal hyperplasia
- **AJCC:** American Joint Committee on Cancer
- **ALH:** Atypical lobular hyperplasia
- **ASCO:** American Society of Clinical Oncology
- **BC:** breast cancer
- **BCS:** breast conservative surgery
- **BM:** bone marrow
- **BMI:** body mass index
- **BRCA1:** Breast Cancer gene 1
- **BRCA2:** Breast Cancer gene 2
- **CDK:** cyclin-dependent kinase
- **CISH:** Chromogenic in situ hybridization
- **CR:** complete response
- **DCIS:** Ductal carcinoma in situ
- **DIN:** Ductal intraepithelial neoplasia
- **DFS:** Disease free survival
- **EGFR:** epidermal growth factor receptor
- **ELISA:** enzyme-linked immunosorbent assay

- **ER:** Estrogen receptor
- **ERK:** Extracellular-signal regulated kinase
- **FOXP3:** Forkhead box P3
- **FISH:** Fluorescence in situ hybridization
- **HER2:** The human epidermal growth factor receptor 2 gene
- **HER/ErbB:** human epidermal growth factor
- **HCPs**: health care professionals
- **HT:** Hormonal therapy
- **H & E:** hematoxilin and eosin staining
- **IARC:** International Agency for Research and Cancer
- **IDC:** invasive ductal carcinoma
- **IHC:** immunohistochemistry
- **IL-10:** interleukin 10
- **(i+):** +ve by IHC
- **Ki-67 LI:** Ki-67 labeling index
- **KRT5:** Keratin, type I cytoskeletal 5
- **KRT:** Keratin, type I cytoskeletal 17
- **LABC:** locally advanced breast cancer
- **LCIS:** Lobular carcinoma in situ
- **LIN:** Lobular intraepithelial neoplasia

- **LN:** lymph node
- **LR:** local recurrence
- **LVI:** lympho-vascular invasion
- **M:** distant metastases
- **MRI:** Magnetic resonance imaging
- **N**: regional lymph nodes
- **NAC**: neoadjuvant chemotherapy
- **NBF:** Neutral buffered formalin
- **NCCN:** National Comprehensive Cancer Network
- **NCI-CU:** National Cancer Institute, Cairo university.
- **NGS:** Nottingham Grading System
- **NOS:** not otherwise specified
- **NSAP:** national surgical adjuvant breast and bowel project
- **NST:** no special type
- **PCR:** polymerase chain reaction
- **pCR:** pathologic complete response
- **PD:** progreassive disease
- **PKB :** Protein Kinase B
- **pNR:** pathological no response
- **pRP:** pathological partial response