Tumour Infiltrating Lymphocytes (TILs) in triple-negative breast cancer:
High immunoscore is associated with pathological CR in patients receiving neoadjuvant chemotherapy

Bl Rapport 1, 2, S Nayler 3, J Galon 4, B Mlecnik 5, T Smit 6, J Barnard-Tidy 7, A Fugon 8, M Martel 9, R. Anderson 10, CA Benn 11

1 The Medical Oncology Centre of Rosebank, Johannesburg, South Africa; 2 Department of Immunology, Faculty of Health Sciences, University of Pretoria, South Africa; 3 Gritzman and Thatcher Inc. Laboratories, Johannesburg, South Africa; 4 Wits Donald Gordon Medical Centre, Johannesburg, South Africa; 5 HalioDx, Marseille, France; 6 Breast Care Centre, Head of Helen Joseph Hospital Breast Centre Johannesburg, South Africa

Introduction

Background

- Neoadjuvant chemotherapy is widely used to downstage breast cancers prior to surgery.

- The immunoscore assay is the first standardized immune-based assay for classification of breast cancer (Hermitte et al., 2016). It assesses the host immune response by measuring intra- and tumour infiltrating lymphocytes.

- Pathological complete response (pCR) rate is a strong predictor of outcome for breast cancer.

Immunoscore®

- The immunoscore assay is the first standardized immune-based assay for classification of breast cancer (Hermitte et al., 2016). It assesses the host immune response by measuring intra- and tumour infiltrating lymphocytes.

Methods

Pathological and clinical assessment

- Clinical assessment of the primary tumour and lymph nodes was made using dimensional ultrasound measurements of the primary tumour and axillary nodes.

- Immunohistochemical staining was performed for ER, PR, HER2 and HER2-neu

- We analyzed data retrospectively/prospectively on 103 breast cancer patients undergoing neoadjuvant chemotherapy.

- Pathological complete response (pCR) was defined as the complete disappearance of the invasive cancer in the breast and absence of tumour in the excised lymph nodes.

- Ethics approval was obtained from Pharma-Ethics, Pretoria, South Africa (ethics committee working according to the South African Ethics regulations).

- NCB software version 11.0 (WitsUSA) was used for statistical analyses.

- Distance assessments: Associations of clinical and pathological characteristics including: ER, HER2, pCR, TILs, C3 and C1 cells/20mm² with pCR.

- All patients were treated with anthracycline and/or taxane-based neoadjuvant chemotherapy.

Immunoscore® Assessment

- In this retrospective analysis, 103 pre-treatment tumour tissue blocks were analysed by immunohistochemical staining for the density (cells/20mm²) of CD3 T-cells, CD8 T-cells, C1 cells, C2 cells, C3 cells and tumours.

- Cohort enrichment through parallel pathological assessments were made.

- Digital pathology dedicated software permitted the measurement of positive cell densities.

- A prognostic classification algorithm was produced to generate a numerical index.

- The median value for each antigen (CD8 + T cells, CD3 + T cells and C1, C2, C3 counts) was calculated in non-pCR and pCR patients.

- Immunoscore® comprises 3 score levels (High, Intermediate, Low).

- Immunoscore® was applied to tumours with immunoscore results and was adopted when no invasion was identified in the specimens.

Statistical Methods

- The primary hypothesis was that higher levels of CD8+ cytotoxic T cells, CD3+ T cells and immunoscore® would be associated with a better overall prognosis, independent of anti-cancer therapy.

- The Mann Whitney U-test was used to compare the cell density between TNBC and non-TNBC patients.

- Fluorescence in situ hybridization (FISH) was used to confirm HER-2 positivity.

- Logistic regression multivariate models included only variables that exhibited a pValue of 0.05 or lower.

- Systemic treatment was defined as the sum of the number of drugs and duration of treatment.

- Significance was considered at p < 0.05.

- Ethics approval was obtained from Pharma-Ethics, Pretoria, South Africa (ethics committee working according to the South African Ethics regulations).

- Statistical analysis (NCBI software version 11.0): WitsUSA was used for statistical analyses.

Conclusions

- Median cell density in patients with pCR vs non-pCR patients

- The median cell density in patients with pCR was significantly higher than non-pCR patients

- Statistical analysis

- Median cell density in patients with pCR vs non-pCR patients

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.

- Significant factors associated with pCR.