

17 **PREDICTIVE SOLUBLE BIOMARKERS OF IMMUNE RESPONSE TO CHECKPOINT BLOCKADE IN NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS**

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**Background** There is limited data on the predictive biomarkers of response to immune checkpoint blockade (ICB) treatment of non-small cell lung cancer (NSCLC) patients. The main aim of this prospective study was to understand the utility of pre-treatment soluble immune checkpoint markers as surrogate markers for tissue PD-L1 and as predictors of response in locally advanced/metastatic NSCLC patients treated with ICBs.

**Methods** The study was conducted at the National Center for Cancer Care and Research (NCCCR), HMC, Qatar. A total of 30 patients on Pembrolizumab/Nivolumab were enrolled and blood samples were collected before treatment. 17 Healthy controls were also included in the study. Multiplex Magnetic Bead Panel kits for soluble immune checkpoint markers was utilized to measure the concentrations of 24 soluble markers including BTLA, GITR, HVEM, IDO, LAG-3, PD-1, PDL-1, PDL-2, TIM-3, CD28, CD80, 4-1BB, CD27, CTLA-4, ICOS Ligand, CD276, VISTA, B7-H6; CD47 (IAP), BLAST-1, Galectin-9, TIMD-4; OX40 and S100A8/A9. Mann-Whitney test was used to evaluate a) the difference in median values between healthy controls and pre-treatment samples b) compare soluble markers with tissue PD-L1 status and c) response to treatment 4 months after treatment via PET CT imaging data.

**Results** The results showed significant changes in the pre-treatment plasma concentrations of soluble markers in the NSCLC patients compared to healthy controls. Significant upregulation was observed in the immune suppression markers: S100A8/A9 (<0.0001\*\*\*), PDL-2 (<0.006\*\*), LAG-3 (<0.006\*\*), PD-1 (<0.008\*), TIM-3 (<0.002\*), CD80 (<0.001\*) and Galactin 9 (<0.023\*). Significant upregulation was observed for the immune stimulatory markers: TIMD4 (<0.0001\*\*\*), CD137/4-1BB (<0.007\*), CD134/OX40 (<0.006\*\*) in NSCLC patients compared to healthy controls. When soluble markers were compared with tissue PD-L1, significant upregulation of CD276/B7-H3 (<0.039\*) and VISTA (<0.034\*) was observed in patients expressing >50% of PD-L1 in their tissues. We then correlated the pre-treatment soluble markers expression with the clinical response of the patients to Pembrolizumab/Nivolumab using imaging (PET CT) data obtained 4 months after treatment. Interestingly, significant upregulation of GITR (<0.0005\*\*\*), PD-L1 (<0.002\*\*) and HVEM (<0.006\*\*) was observed in responding patients.

**Conclusions** The study demonstrates that 10 markers show differences in NSCLC patients as compared to healthy controls; 2 markers as surrogates for tissue PDL-1 and 3 markers as predictive biomarkers of response to ICB treatment.

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**Ethics Approval** The study was approved by Hamad Medical Corporation, Medical Research Center Ethics Board; approval number MRC-01-20-507

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