Serum Immune Checkpoint biomarkers as predictors response to anti-PD-1/PD-L1 treatment in Non-Small Cell Lung Cancer (NSCLC) patients

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Background
Targeted therapy in Non-small cell lung cancer (NSCLC) with immune checkpoint inhibitors (ICIs) Nivolumab/Pembrolizumab have been associated with better overall survival. 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 is to understand the utility of pre-treatment soluble immune checkpoint and tumor markers as early 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 26 patients on anti-PD-1/PD-L1 were enrolled, and blood samples were collected before treatment. Multiplex Magnetic Bead Panel kits for soluble immune checkpoint markers was utilized to measure the concentrations of soluble immune checkpoint and tumor 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, S100A8/A9, E-cadherin, MICB, Nectin 2, NTSE, PVR, Singlec 7, Singlec 9, CEA, CA-19-9, CA-125 CYFRA21-1 and CA-15-3.

Mann-Whitney test was used to evaluate response to treatment 4 months after initiation of treatment via PET CT imaging data.

Results
Clinical response to ICB treatment was determined based on RECIST criteria and PET CT imaging data. 12/26 (46%) patients showed clinical response to the treatment while 14/26 (54%) were identified as non-responders.

Interestingly, in clinically responding patients, significant upregulation of the immune inhibitory soluble programmed death-ligand 1 (sPD-L1) molecule (<0.002**) and the immune stimulatory biomarkers glucocorticoid-induced TNFR-related protein (GITR) (<0.0005**) were recorded. However, non-responding patients showed significant upregulation of 3 important immune suppressive biomarkers; T-cell immunoglobulin and mucin domain containing 4 (TIMD-4) (p<0.0361*), Nectin 2 (p<0.0310*) and the carcinoembryonic antigen (CEA) tumor marker (p<0.0484*).

Conclusion
The study gives evidence of upregulation of soluble immune suppressive and stimulatory biomarkers in responding and non-responding patients indicating their utility as plausible early biomarkers of response to treatment.

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

I declare no conflict of interest

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