A064 Novel Autoantibodies Biomarkers Panel Test to Prognosticate Clinical Outcomes in Advanced-stage NSCLC Patients Receiving Anti PD-1/-L1 Immunotherapy
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Introduction: Lung cancer is the leading cause of cancer-related deaths worldwide, with a vast majority of cases presenting at an advanced, metastatic stage. Anti PD-1/-L1 immunotherapy has transformed clinical outcomes in non-small cell lung cancer (NSCLC), however, the overall response rate for these patients remains sub-optimal. With this, the objective of this study was to develop improved methods for prognosticating clinical response in these patients based on pre-treatment circulating autoantibody signatures. Methods: Pretreatment sera from two outcome groups (“Poor” response, n=20, overall survival <12 months; “Good” response, n=20, overall survival >12 months) were evaluated via the HuProt™ Human Proteome Microarray (CDI laboratories, Baltimore, MD) to functionally identify prognostic neoantigens. A total of 145 neoautoantigen targets were identified with ≥2 fold change in titer levels and a p≤0.02. Custom ‘indirect’ immunobead assays were then developed on the Luminex platform for the 13 most promising candidate biomarkers using standard NHS-carbodiimide chemistries with recombinant neoautoantigens. The resulting 13-plex assay was then used to quantify pretreatment autoantibody titers in a cohort of 125 metastatic NSCLC patients receiving anti PD-1/-L1 agents. Statistical association of autoantibody titers with clinical outcomes, including progression free survival (PFS), overall survival (OS), and grade III adverse events, was then accomplished using Cox regression. Results: The results from our analytical validation studies demonstrated all assays had excellent precision (<10 %CV), low (<5%) cross reactivity, and dynamic range over five order of magnitude. Clinically, low baseline titers of ZNF695, MCM4, PRMT2, FGD3, GTF2A1, GLUL, CDCA3, ZNF277, GARS, GBP2, UBL7, and ASNA1 autoantibodies were associated with a longer PFS (all p-values <0.01), whereas increased titers were associated with an inferior PFS outcome (0.06, HR=0.66, 95% CI). Low titers of ZNF695, MCM4, PRMT2, FGD3, GARS, GBP2, and UBL7 autoantibodies were associated with a favorable OS (all p-values <0.01). Conclusion: In this study, we provide compelling ‘proof-of-principle’ evidence that circulating autoantibodies have great promise for prognosticating therapy response in advanced NSCLC patients receiving anti PD-1/-L1 immunotherapy. Upon further validation, this approach may provide a basis for improved methods to help guide treatment decisions for patients with advanced NSCLC.