UTILIZING SERUM PROTEOME TO UNDERSTAND RESPONSE AND RESISTANCE TO IMMUNE CHECKPOINT INHIBITORS IN ADVANCED NON-SMALL CELL LUNG CANCER

¹Leeseul Kim*, ²Young Kwang Chae, ²Dong-Uk Lee. ¹AMITA Health Saint Francis Hospital Evanston, Chicago, IL, USA; ²Developmental Therapeutics Northwestern Medicine, Chicago, IL, USA

Background Predictive biomarkers are more in need considering that responses and resistance to immune checkpoint inhibition (ICI) are poorly understood. We used a validated serum-based proteomic test, Primary Immune Response (PIR), to predict response and Protein Set Enrichment Analysis (PSEA) scores to elucidate mechanisms of early resistance to ICI in patients with advanced non-small cell lung cancer (NSCLC). (Muller et al., 2020)

Methods Serum of 43 consented NSCLC patients was collected prospectively at 2 timepoints: baseline (prior to ICI initiation) and 3 weeks after ICI initiation (median 22 days). Blinded samples were classified by the PIR test. Clinical response was evaluated using RECIST. Outcomes, including progression-free survival (PFS) and overall survival (OS), were analyzed by PIR classifications as intermediate/sensitive (not resistant) vs. resistant at baseline and 3 weeks. Multivariable regression was performed. PSEA scores indicating activity of 10 processes of interest (e.g., Type 1 immunity (Th1), complement, interferon-gamma (IFN γ)) were compared between PIR groups.

Results Of the 43 patients, 28 received chemotherapy with ICI (chemo+ICI) and 15 received ICI alone. 31 of 43 patients (72%) were treatment naïve at baseline blood draw. PIR-resistant patients had worse survival compared to patients classified as not resistant (HR, 10.4; 95%CI, 1.3–81 ; P = 0.025). OS was also significantly lower for patients with PIR resistant result at 3 weeks (HR, 9.1; 95%CI, 1.2–72 ; P = 0.036). The difference in survival between PIR classification groups was consistently observed in the treatment naïve patients treated with chemo+ICI (log rank P = 0.02). No significant differences were observed in PFS. Clinical and pathologic characteristics, including PD-L1 expression, were not significantly associated with PIR result. In multivariable analysis including performance status, line of therapy, and PD-L1 status, PIR resistant remained a significant negative prognostic factor (HR, 8.2; 95%CI, 1.01–67; P = 0.049). PSEA scores at baseline and 3 weeks after ICI initiation showed significantly higher levels of complement, IFN γ , Th1, immune tolerance, and a lower level of wound healing (all P<0.0001) in PIR-resistant vs. PIR-intermediate/sensitive.

Conclusions These data further validate the utility of the PIR test in predicting patient survival on ICI. Processes associated with PIR resistant result included activation of complement, IFN γ , Th1, and immune tolerance, elucidating early mechanisms of resistance to ICI in a clinical cohort.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.269>