SERUM PROTEOMICS SIGNATURE AND ITS ASSOCIATION WITH IMMUNE-RELATED TOXICITIES AND SURVIVAL IN PATIENTS WITH NON-SMALL CELL LUNG CANCERS (NSCLC) RECEIVING IMMUNOTHERAPY

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Background The circulating proteome, which reflects the host’s response to diseases, is currently being investigated as a potential marker to assess the response to immune checkpoint inhibitors (ICI). However, early detection and recognition of immune-related adverse events (irAEs) of ICI are equally crucial. There is a high unmet need to develop serum-based biomarkers that can accurately predict irAEs.

Methods In this retrospective study, we employed a proteomics assay (VeriStrat, Biodesix) that utilizes machine learning algorithms and MALDI-ToF mass spectrometry-based signatures. A total of 105 patients diagnosed with NSCLC who received ICI therapy as neoadjuvant, adjuvant, or palliative treatment, either as monotherapy or in combination with chemotherapy, were included. Proteomics assay was performed on blood samples collected between 2018 and 2023, and patients were classified into two groups based on their assay scores: VeriStrat Good (VS-G) and VeriStrat Poor (VS-P). The log-rank test was used to analyze the time to occurrence of the irAE.

Results Among 105 patients analyzed, 42 received ICI-only regimens, while 63 received ICIs in combination with cytotoxic chemotherapy. Of these patients, 87 received palliative immunotherapy, 9 received neoadjuvant immunotherapy, and 9 received adjuvant immunotherapy. A total of 27 patients (25.7%) experienced irAEs, with 3 patients experiencing grade ≥ 3 irAEs. Among those who developed irAEs, 7 developed pneumonitis, 5 developed rash, 2 developed hypophysitis and developed colitis respectively. Among 86 patients in the VS-G group 20 developed irAEs (23.3%), but 7 out of 19 people in the VS-P group developed irAEs (36.8%). The VS-P group demonstrated a tendency to develop toxicities earlier than those in the VS-G group (hazard ratio [HR]=2.13; 95% confidence interval [CI], 0.88–5.16; P = 0.08) (figure 1A).

VS-P showed a trend for poorer survival compared with VS-G patients, although not statistically significant (HR=1.57; 95% CI, 0.70–3.56) (figure 1B).

Conclusions We report for the first time that the VS-P group may develop earlier toxicity compared to the VS-G group. This finding may provide a proof-of-concept that serum proteomics reflecting the host immune environment may help predict irAE with ICI use. Furthermore, identifying VS-P group associated with inferior efficacy-toxicity ratio may be of clinical significance in immune-oncology. Further validation in a larger cohort is warranted.

Ethics Approval Northwestern IRB approved: STU00207117