

# P3.109: Olink-Based Plasma Proteomic Dynamics and Prognostic Modeling in Elderly Patients With Advanced NSCLC Receiving First-Line Immunotherapy

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## INTRODUCTION

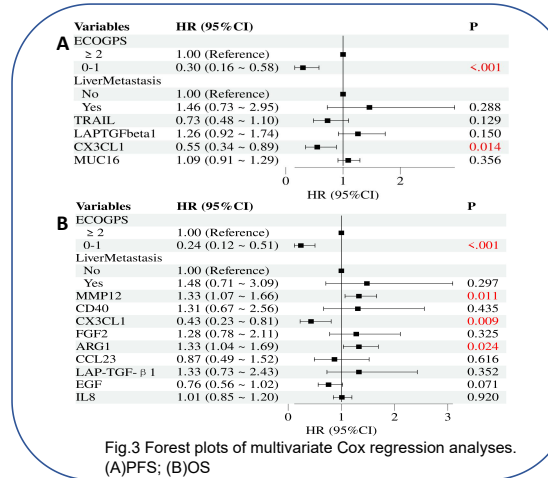
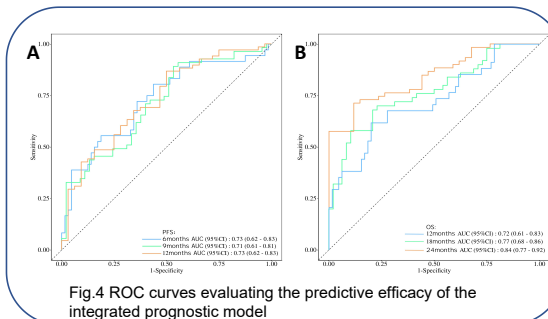
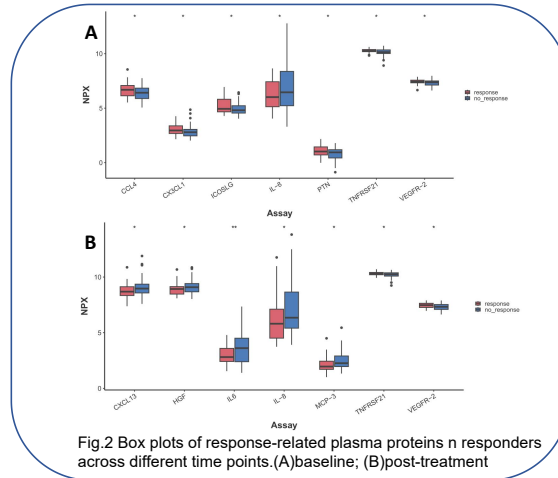
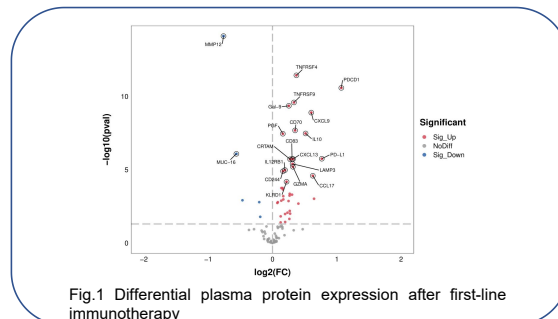
- Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of advanced non-small cell lung cancer (NSCLC) in elderly patients; however, only a subset derives durable benefit, and the lack of predictive and prognostic biomarkers remains a key clinical challenge.
- To address this, we aimed to characterize dynamic plasma proteomic changes using Olink assays, identify candidate proteins associated with treatment response and survival, and develop and internally validate prognostic models.

## METHODS

We collected paired plasma samples from 100 elderly patients with advanced NSCLC at baseline and after two cycles of first-line immunotherapy. Plasma levels of 92 proteins were profiled using the Olink platform. Dynamic proteomic changes associated with treatment exposure and response were evaluated, followed by exploratory analyses of proteins associated with progression-free survival (PFS) and overall survival (OS). Based on candidate prognostic proteins and clinical variables, internally validated prognostic models were developed to estimate survival outcomes in elderly patients receiving first-line immunotherapy.

## RESULTS

- In elderly advanced NSCLC, 45 of 92 quantified plasma proteins significantly changed following first-line immunotherapy ( $p < 0.05$ ), enriched in immune and inflammatory signaling pathways (Fig.1).
- Responders exhibited higher baseline CCL4, CX3CL1, ICOSLG, PTN, TNFRSF21, VEGFR-2 and lower IL-8. Post-treatment increases in CXCL13, HGF, IL-6, IL-8, MCP-3 predicted poor response, whereas elevated TNFRSF21 and VEGFR-2 predicted favorable response (all  $p < 0.05$ ) (Fig.2).



## RESULTS

- Survival analysis identified CX3CL1 as an independent protective biomarker, with high levels correlating with longer PFS (HR=0.55,  $P=0.014$ ) and OS (HR=0.43,  $P=0.009$ ). Elevated ARG1 and MMP12 indicated higher mortality risk (Fig.3).
- Integrative clinical-biomarker prognostic models were internally validated, achieving AUCs of 0.73/0.71/0.73 (6/9/12-month PFS) and 0.72/0.77/0.84 (12/18/24-month OS) (Fig.4).

## DISCUSSION AND CONCLUSION

- Dynamic plasma proteomic profiling revealed immune-related molecular changes after immunotherapy in elderly NSCLC patients.
- A prognostic model incorporating CX3CL1, ARG1, MMP12, and clinical factors effectively predicts survival in elderly patients with advanced NSCLC receiving immunotherapy, warranting further validation.
- Our findings support Olink-based plasma proteomics as a promising liquid biopsy approach for biomarker discovery and personalized immunotherapy in the elderly population.