

EP03.10. Metabolic, Lipid, and Inflammatory Biomarkers as Predictors of Response and Survival to ICIs in Advanced NSCLC

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INTRODUCTION

Despite improved outcomes with immune checkpoint inhibitors (ICIs) in advanced non-small cell lung cancer (NSCLC), **predictive biomarkers remain limited**. We investigated metabolic, lipid-related, and inflammatory biomarkers associated with treatment response and resistance.

METHODS

Design: Prospective observational study in advanced NSCLC patients treated with ICIs ± chemotherapy.

➤ **Sample collection:**

Blood samples were collected at **V0** (baseline) and **V1** (9 ± 3 weeks after treatment initiation).

➤ **Clinical and biomarker assessment:**

In addition to clinical-pathological variables and routine laboratory parameters, including lipid profile, **potential biomarkers were assessed at V0 and V1**, with particular attention to **fatty acids, adipokines, and cytokines**.

➤ **Data analysis:**

•**Artificial intelligence** (AI)-based biomarker-response analysis comparing responders (Rs; complete response [CR] or partial response [PR]) vs non-responders (NRs; stable disease [SD] or progressive disease [PD]);
•**Kaplan-Meier** (KM; log-rank test) and **univariate Cox regression analyses** for survival outcomes (progression-free survival [PFS] and overall survival [OS]).

RESULTS

Study population:

23 patients with advanced NSCLC were included (median age: 70 years; range: 55-83).

Beyond the expected metabolic differences between Rs and NRs (NRs, V1: ↑LDL, ↑triglycerides, ↓HDL; Rs: ↑hypercholesterolemia/statin use), **distinct biomarker profiles emerged from AI-based analyses of fatty acids, adipokines, and cytokines**. **Selected biomarkers** from these classes **were also associated with OS or PFS**, either significantly (p<0.05) or with a trend toward significance (0.05≤p<0.10).

1) FATTY ACID RESULTS

AI: Stearic acid (C18:0), V0: ↓ levels in Rs vs NRs; p=0.04 (**Figure 1A**). **Cox regression analysis: Palmitic acid (C16:0), V0:** ↑ levels → shorter OS; HR=1.36, 95% CI 0.98–1.87; p=0.07. **Arachidonic acid (C20:4), V0/V1:** ↑ levels → longer OS; V0: HR=0.51, 95% CI 0.25–1.03; p=0.06; V1: HR=0.71, 95% CI 0.49–1.05; p=0.09. **Linoleic acid (C18:2), V1:** ↑ levels → shorter PFS; HR=1.14, 95% CI 0.98–1.32; p=0.08. **KM analysis: Arachidonic acid (C20:4), V0:** ↑ levels → longer OS; median OS: 30.01 vs 14.65 months; p=0.05 (**Figure 1B**).

2) CYTOKINE AND ADIPOKINE RESULTS

AI: Adiponectin, V1: ↓ levels in NRs; p=0.06 (**Figure 2A**). **Cox regression analysis: Visfatin, V1:** ↑ levels → longer PFS; HR=0.58, 95% CI 0.33–1.02; p=0.06. **IFN-γ, V0/V1:** ↑ levels → shorter OS; V0: HR=1.18, 95% CI 0.98–1.42; p=0.07; V1: HR=1.51, 95% CI 0.95–2.42; p=0.09. **IL-10, V1:** ↑ levels → shorter PFS; HR=1.07, 95% CI 1.00–1.14; p=0.04. **KM analysis: Visfatin, V1:** ↑ levels → longer PFS; median PFS: 15.15 vs 8.80 months; p=0.03 (**Figure 2B**).

Cox: continuous biomarker levels; KM/log-rank: biomarkers dichotomized by median (≥ vs < median).

DISCUSSION AND CONCLUSION

Actionable Take Away Message

An integrated blood-based metabolic, lipid-related, and inflammatory profiling approach revealed distinct biological patterns between Rs and NRs and identified biomarkers associated with clinical outcomes in advanced NSCLC treated with ICIs ± chemotherapy.

Future Direction for Research

Prospective multicenter validation is required to confirm these biomarker associations, refine AI-based response prediction models, and assess their **potential role in patient stratification and personalized immunotherapy**.

REFERENCES & ACKNOWLEDGEMENTS

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