



INTRODUCTION

- Concurrent chemoradiotherapy (CRT) followed by durvalumab is the standard of care in unresectable stage III NSCLC, yet many patients derive no durable benefit.
- Tumour- and radiotherapy-induced systemic inflammation and immunosuppression (MDSC expansion, lymphocyte depletion) may limit immunotherapy efficacy.
- Neutrophil-to-lymphocyte ratio (NLR) and absolute lymphocyte count (ALC) are simple, routinely available markers of this immune state.
- We hypothesised that combining both captures prognosis better than either alone.

METHODS

- Retrospective study of 100 patients with stage III NSCLC treated with definitive CRT; analysis focused on the durvalumab subgroup (n=24).
- Pre-RT NLR from blood counts before the start of radiotherapy (cut-off ≥ 3).
- Post-RT ALC defined as the lymphocyte nadir within 4 weeks after completion of radiotherapy (cut-off $\leq 1000/\mu\text{L}$).

Combined immuno-inflammatory score

- High risk = elevated inflammation (NLR ≥ 3) AND immunosuppression (ALC $\leq 1000/\mu\text{L}$).
- Non-high risk = all other patients.
- PFS and OS estimated by Kaplan-Meier and compared by log-rank test; Cox proportional hazards models for multivariable analysis.

DISCUSSION AND CONCLUSION

- A combined score based on pre-RT NLR and post-RT ALC stratified both OS and PFS in stage III NSCLC treated with CRT followed by durvalumab.
- The score remained associated with survival in multivariable analysis, suggesting prognostic information beyond PD-L1 expression.
- Findings support a role for the interplay between systemic inflammation and treatment-induced immunosuppression in shaping response to immunotherapy.

Actionable take-away

- Two routine blood parameters, available at no additional cost, identify a high-risk group with a median OS of only 15.9 months despite consolidation durvalumab.

Future directions

- Prospective validation in larger cohorts, and evaluation of lymphocyte-sparing radiotherapy planning to reduce post-RT lymphopenia.

REFERENCES & ACKNOWLEDGEMENTS

Acknowledgements & disclosures

- No conflicts of interest to declare.
- Reference list available from the corresponding author: fguerre@institutoaroffo.uba.ar



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RESULTS

- 24 patients; 58% male; median age 69.9 years (IQR 62-72). High risk 10 (42%), non-high risk 14 (58%). Median follow-up 27.4 months.
- Median PFS 6.7 months (high risk) vs not reached (non-high risk), $p < 0.001$. Median OS 15.9 months vs not reached, $p = 0.0025$.
- Multivariable Cox: combined score HR 0.18 (95% CI 0.03-0.97; $p = 0.046$); PD-L1 HR 0.20 (95% CI 0.04-1.04; $p = 0.056$).

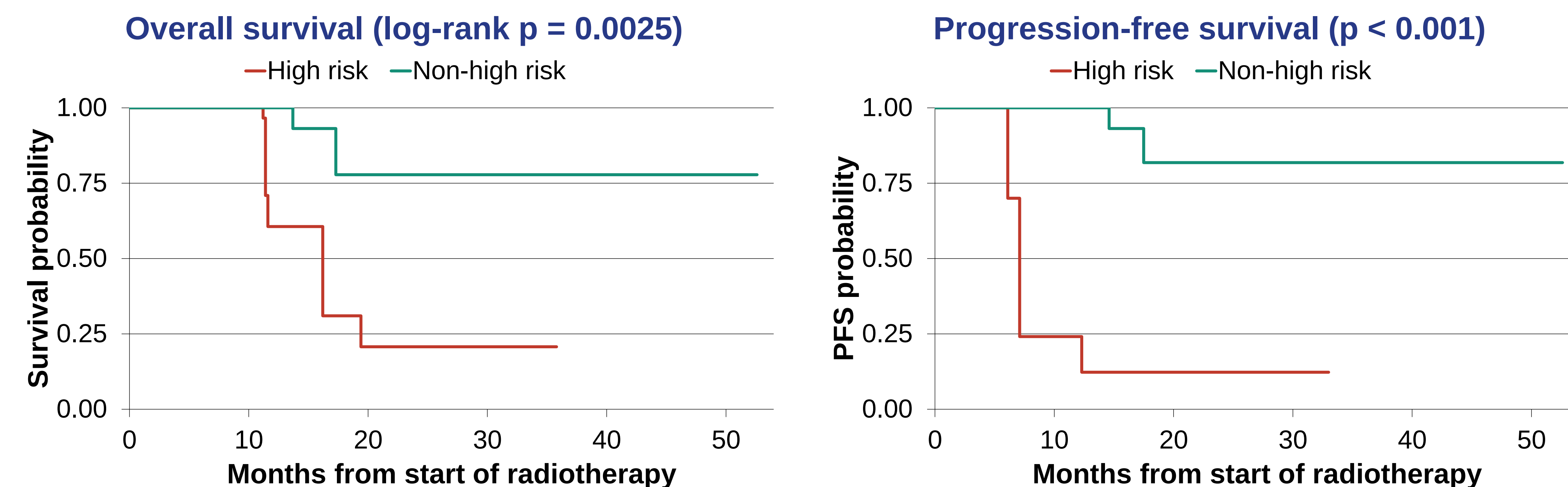


Table 1. Baseline characteristics by combined immuno-inflammatory score

Characteristic	High risk (n=10 ¹)	Non-high risk (n=14 ¹)	p^2
Age, years — median (IQR)	62 (43–72)	70 (63–72)	0.11
Male sex — n (%)	9 (90%)	5 (36%)	0.013
Stage IIIA / IIIB	6 / 4	4 / 10	0.20
Squamous / Adeno / NOS	4 / 2 / 4	2 / 11 / 1	0.017
PD-L1 <1% / 1–49% / $\geq 50\%$ / NT	7 / 1 / 0 / 2	3 / 1 / 6 / 4	0.036
Pre-RT NLR — median (IQR)	3.65 (3.18–5.20)	2.26 (1.90–2.67)	0.003
Pre-RT NLR ≥ 3 — n (%)	10 (100%)	3 (21%)	<0.001
Baseline ALC, μL	1,800 (1,420–1,910)	2,200 (1,722–2,670)	0.026
Post-RT ALC, μL	580 (480–703)	1,155 (450–1,500)	0.043
Post-RT ALC $\leq 1000/\mu\text{L}$ — n (%)	10 (100%)	5 (36%)	0.002

¹Median (Q1-Q3); n (%)

²Wilcoxon rank sum test; Fisher's exact test