



Re-evaluation of inflammatory modification and exploration of longitudinal PET metabolic changes

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INTRODUCTION

CLINICAL QUESTION

Does systemic inflammation (PLR) modify the prognostic value of PET metabolic tumour volume (MTV) after neoadjuvant chemoimmunotherapy?

- Cut-point-defined interactions can be unstable and require continuous-variable confirmation.
- We formally reassessed PLR×MTV and explored whether longitudinal primary-tumour ΔSULpeak better reflects pathological response.

METHODS

DESIGN AND COHORTS

Setting: single-centre retrospective stage III NSCLC; no detected baseline EGFR-sensitising mutation or ALK rearrangement.
Treatment: ≥2 cycles of ICI plus platinum chemotherapy, followed by R0 surgery.
Nested cohorts: overall n=92; continuous RECIST n=88; baseline cN-positive n=75.

ANALYSES

Prognosis: continuous PLR×MTV Cox interaction (n=88; 32 events), likelihood-ratio testing, Holm correction and bootstrap.
PET response: primary-tumour ΔSULpeak, ΔTLG and ΔMTV; positive values indicate reduction.
Endpoints: MPR (RVT≤10%), pCR, continuous RVT, ypN0 and nodal downstaging.
Statistics: empirical ROC/AUC, 20,000 patient-level bootstrap resamples and conditional partial-rank correlations.

DISCUSSION AND CONCLUSION

BOTTOM LINE

The PLR–MTV interaction was not confirmed. Exploratory primary-tumour ΔSULpeak consistently signalled pathological response.

- 1 Correction.** Continuous PLR×MTV analyses did not reproduce the original inflammatory-modification hypothesis.
- 2 Response.** Longitudinal ΔSULpeak was the clearest primary-tumour signal for MPR and outperformed RECIST.
- 3 Boundary.** The signal was weaker for ypN0; nodal pathology remains essential.
- 4 Next step.** External validation is required before clinical use.

TAKE-HOME MESSAGE

NOT CONFIRMED — PLR×MTV inflammatory modification
NEW SIGNAL — longitudinal primary-tumour ΔSULpeak for pathological response
CLINICAL BOUNDARY — nodal pathology remains essential

EVIDENCE SUMMARY

ORIGINAL HYPOTHESIS

Continuous PLR×MTV interactions were not confirmed: baseline P=0.487; preoperative P=0.415; Holm-adjusted P=0.830 for both.

LONGITUDINAL PET RESPONSE

Primary-tumour ΔSULpeak identified MPR (AUC 0.852; 95% CI 0.767–0.925). In the paired cohort, AUC was 0.860 versus 0.649 for RECIST, with paired ΔAUC 0.211 (95% CI 0.073–0.350).

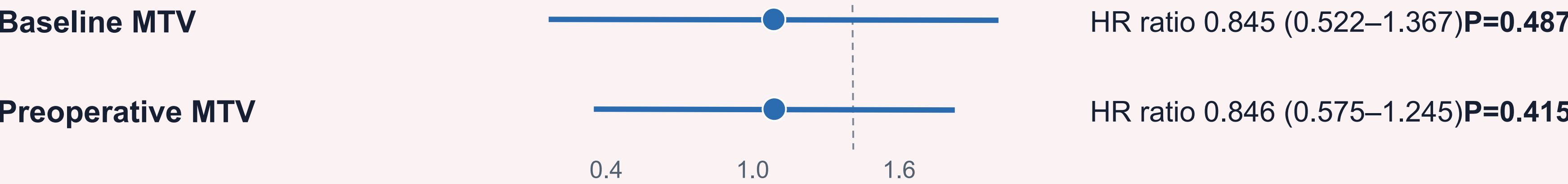
CLINICAL BOUNDARY

Among 75 cN-positive patients, ΔSULpeak was more informative for MPR (AUC 0.842) than ypN0 (AUC 0.703). Conditional association ≈ 0 after accounting for primary pathology; nodal pathology remains essential.

RESULTS

Formal re-evaluation of the PLR×MTV prognostic interaction

Frozen prognostic cohort: n=88; 32 postoperative events

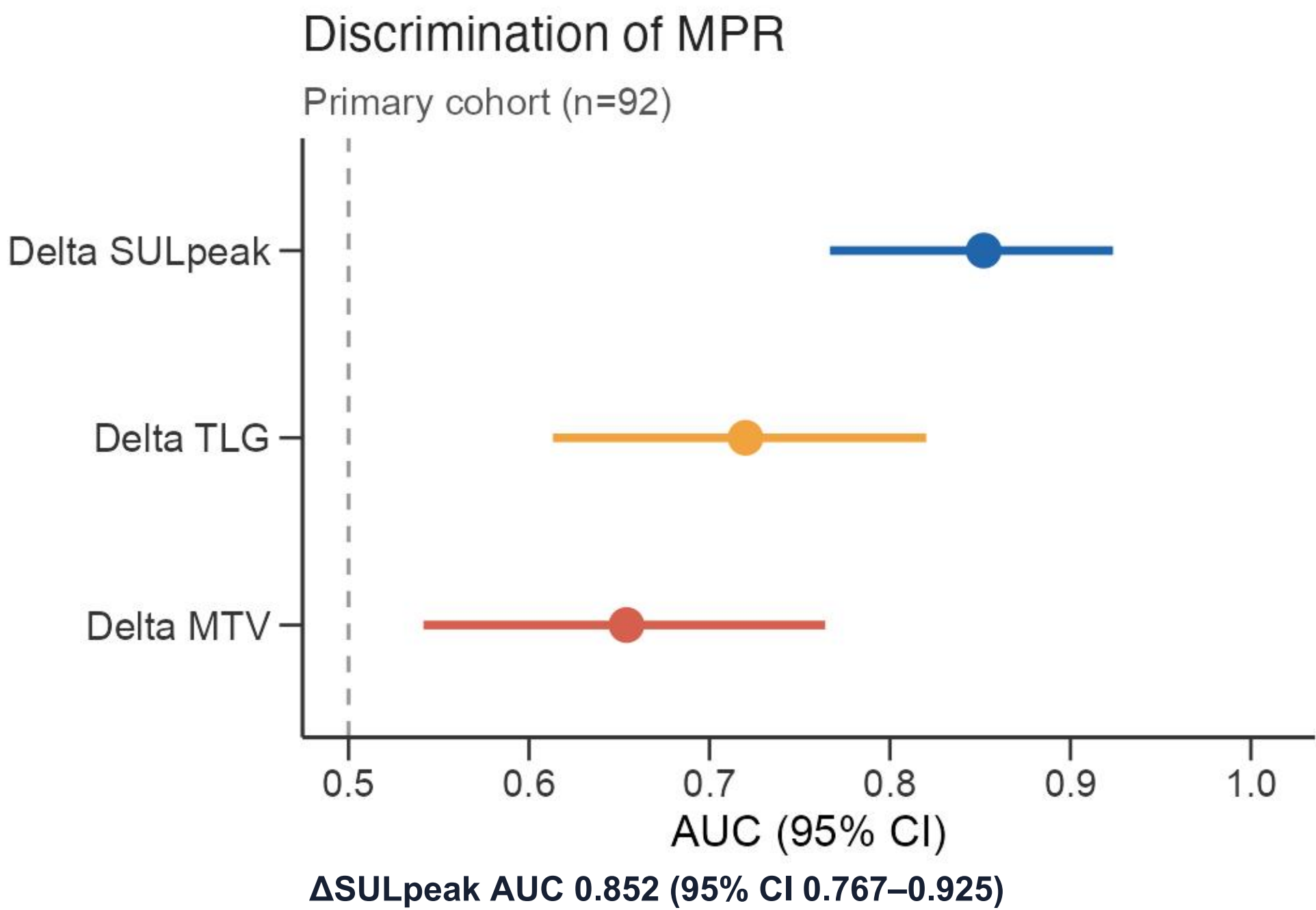


NOT CONFIRMED
Holm-adjusted P=0.830 for both

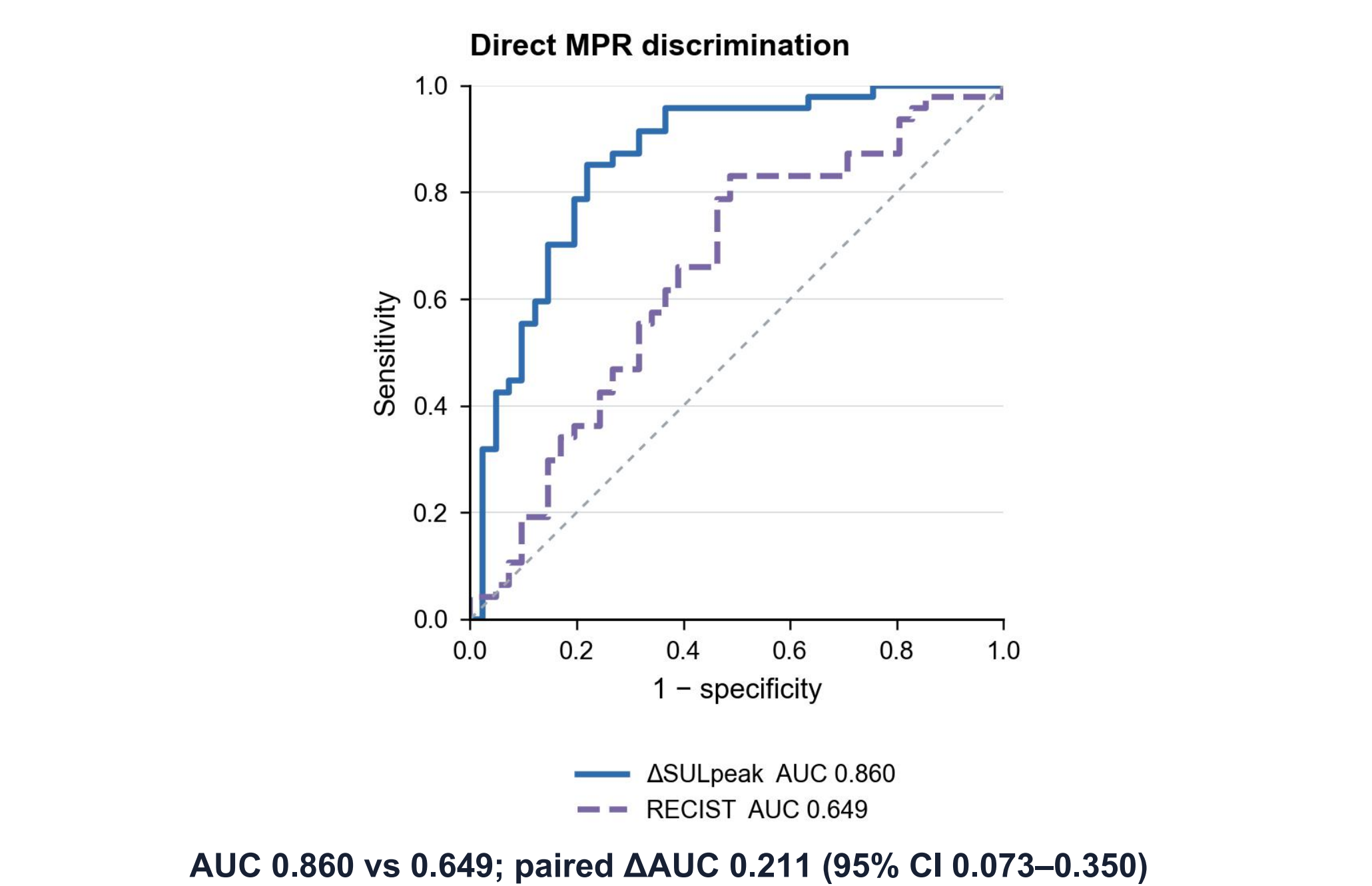
EXPLORATORY METABOLIC-RESPONSE ANALYSIS

53.3% MPR (49/92)
34.8% pCR (32/92)
82.7% N downstaging

A ΔSULpeak outperformed volumetric PET metrics



B ΔSULpeak added information beyond RECIST



C Primary and nodal pathological responses can diverge

Baseline cN-positive cohort (n=75): the same primary-tumour ΔSULpeak was more informative for MPR than for ypN0.

