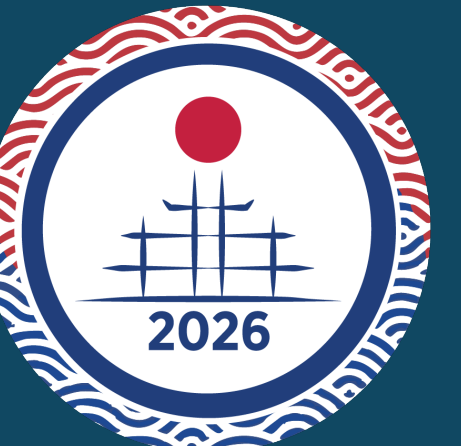


Neoadjuvant Single-Dose Atezolizumab in Resectable IA-IIIA NSCLC: Immune-Profilng and Transcriptomic Analyses From Phase 2 PRINCEPS Trial

P1.120



IASLC
WCLC 2026

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HIGHLIGHTS

One dose reshapes circulating immunity within 15 days

Residual tumour inversely tracks with adaptive immune activation

Blood scores separate outcomes only in treated patients

METHODS

- PRINCEPS (NCT02994576) is a phase 2 trial of one neoadjuvant atezolizumab cycle in resectable NSCLC, with an upfront-surgery control cohort.
- Blood was profiled at D0/D15 by multiparametric flow cytometry (194 features).
- Tumours were profiled by flow cytometry, IHC and bulk RNA-seq.
- Composite blood scores were derived in treated patients using Cox/Spearman screening, stability-based selection and biological de-duplication, with robustness assessed by multivariable Cox, bootstrap, permutation testing and frozen application to untreated controls.

CONCLUSIONS

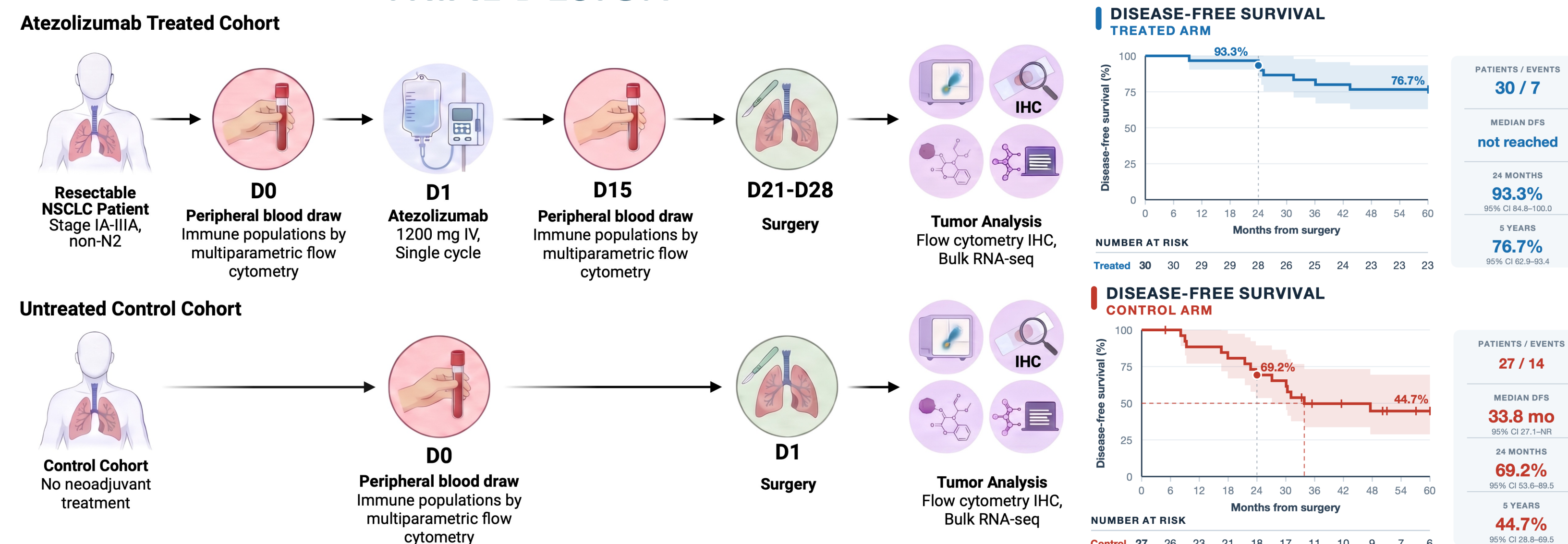
One neoadj. atezolizumab cycle induces coordinated peripheral immune remodelling within 15 days, with increased T-cell costimulation, myeloid Fcγ receptors, NK-cell expansion, contraction of senescent CD57⁺ NK cells, Treg activation.

In tumours, RVT is inversely associated with TLS and IFN-γ/T-cell-inflamed signatures.

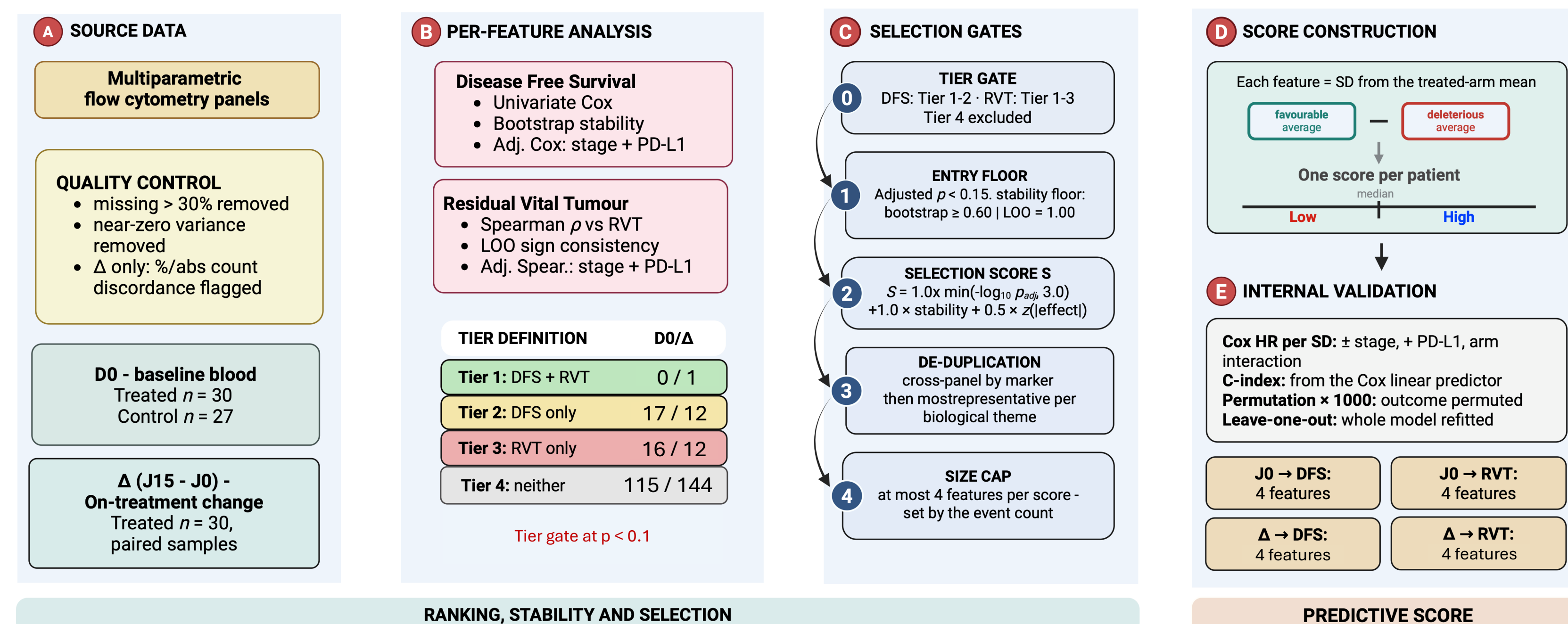
Composite immune scores separate DFS and correlate with residual tumour in treated patients, but not in controls, supporting a treatment-specific rather than prognostic signal.

These exploratory, internally derived scores require independent validation.

TRIAL DESIGN

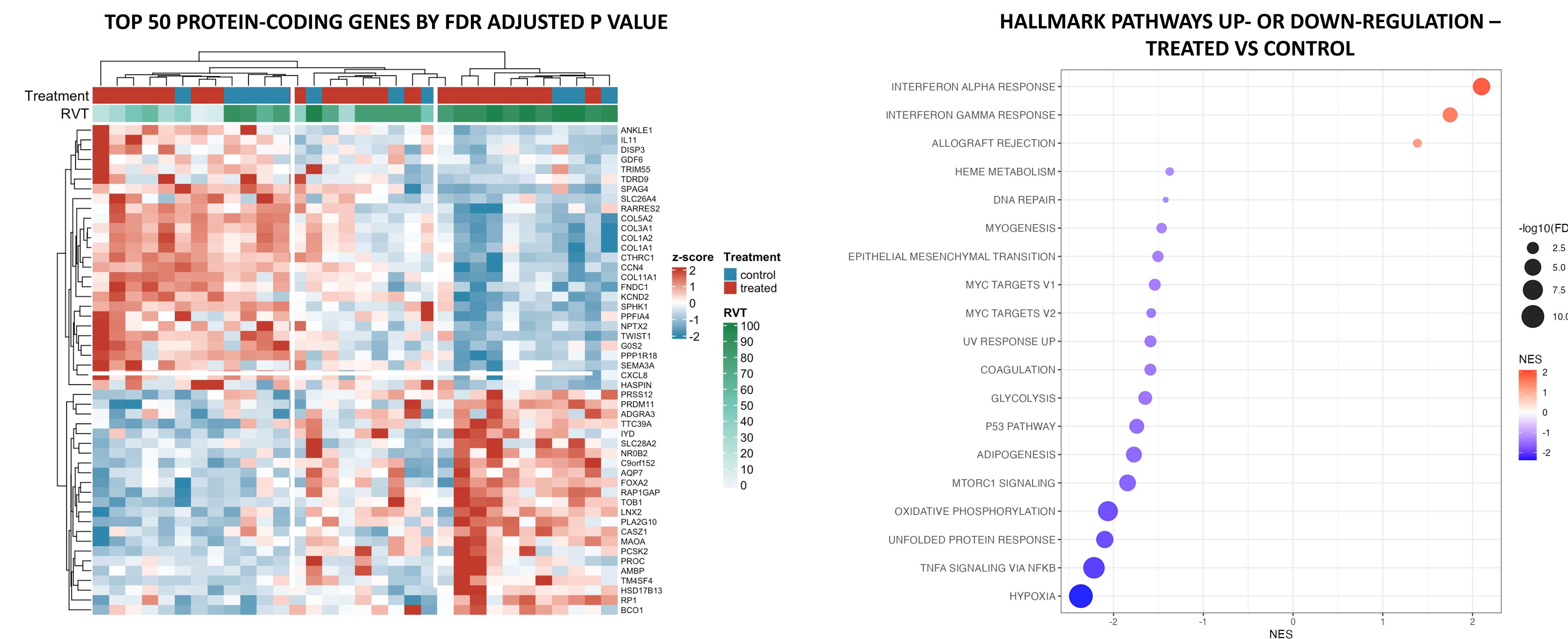


CIRCULATING IMMUNE PREDICTIVE SCORES FOR RVT AND DFS

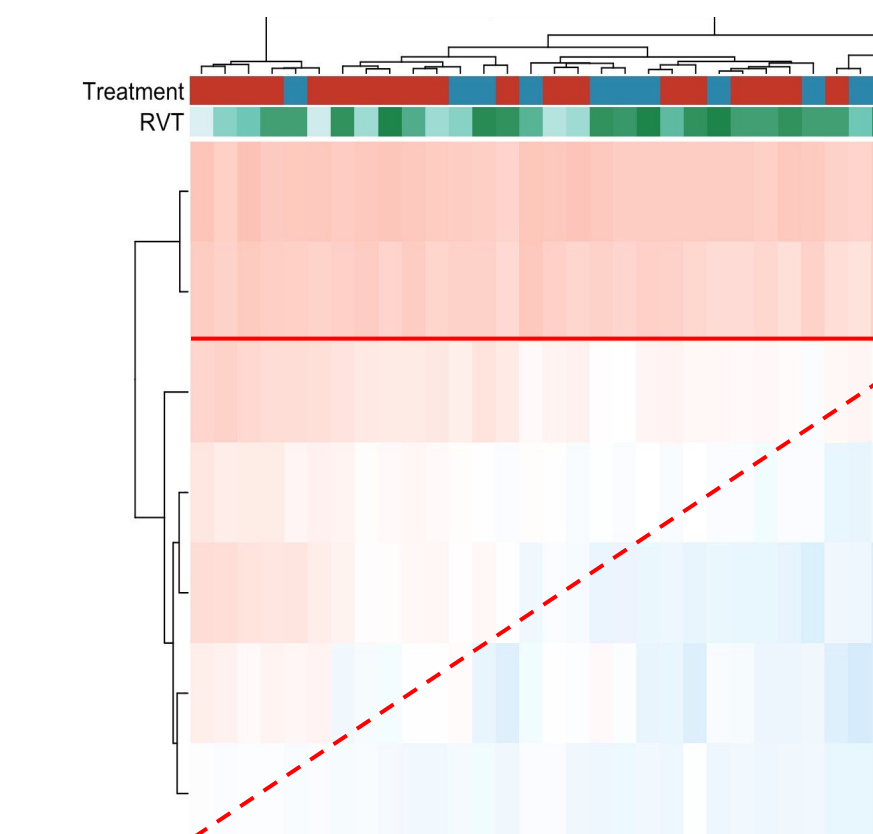


RESULTS

TRANSCRIPTOMIC ANALYSIS, PATHWAYS ENRICHMENT AND IMMUNE-DECONVOLUTION



IMMUNE SIGNATURES

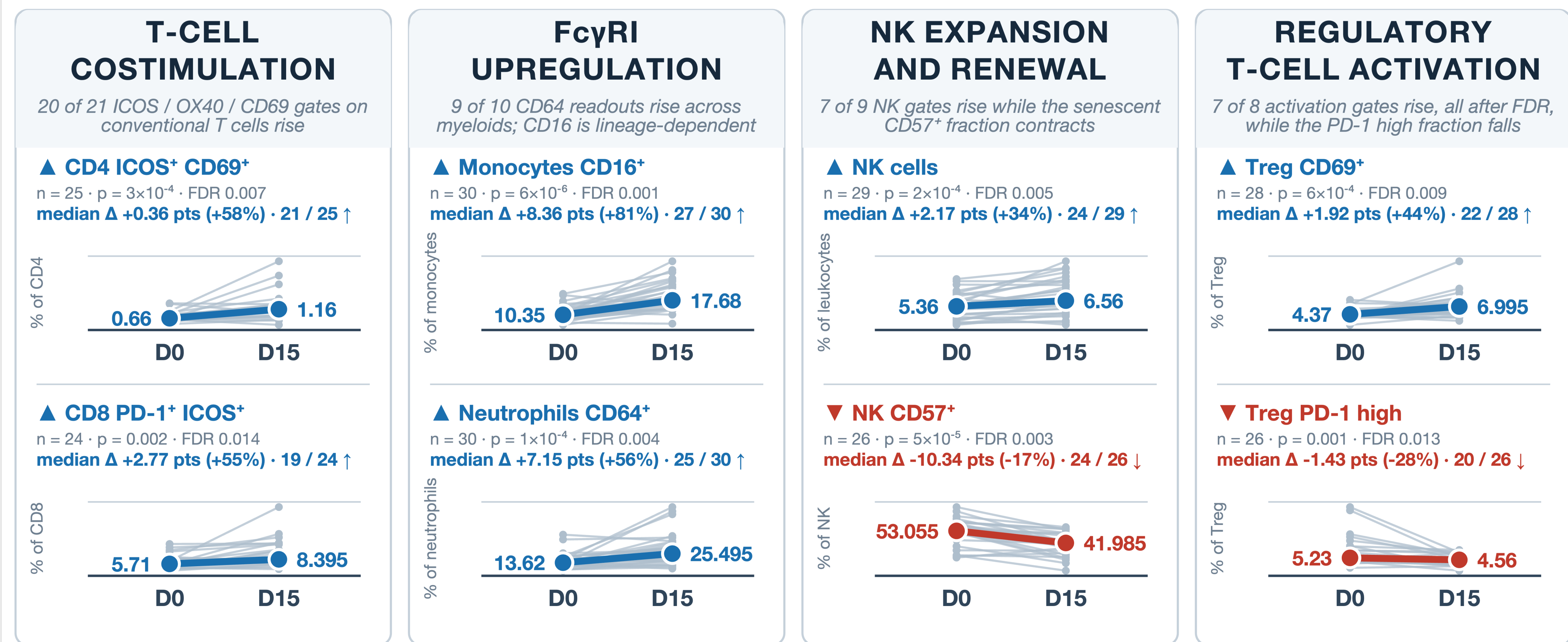


Immune Signature	Spearman rho	p-value	BH correction
TLS	-0.577	0.0005	0.0035
Inflamed T cells	-0.543	0.0013	0.0046
IFN gamma	-0.473	0.0063	0.0147
M1 macrophages	-0.403	0.0222	0.039
Exhausted T cells	-0.386	0.0293	0.041
TGF beta	-0.356	0.0454	0.053
M2 macrophages	-0.253	0.163	0.163

RNA-seq analysis (21 Treated, 11 Ctrl): IFN-α/γ pathways enrichment in Treated tumours cells, with depletion of hypoxia, OxPhos and mTORC1 programs.

Immune deconvolution: TLS, T-cell-inflamed and IFN-γ signatures correlated negatively with RVT, while stromal/CAF programs correlated positively.

PERIPHERAL ACUTE IMMUNE RESPONSE TO ONE CYCLE OF ATEZOLIZUMAB



- Baseline D0 → DFS/RVT:** lymphoid-rich, low-inflammation profile (↑ CD3⁺ T cells, ↓ NLR), with costimulation-competent OX40⁺ CD4 cells and fewer exhausted CD244⁺ cells / activated ICOS⁺ CD69⁺ Tregs → **better outcome**.
- Δ(D15–D0) → DFS:** ↑ antigen-presenting HLA-DR⁺ monocytes, activation-induced Tim-3⁺ CD8 T cells and PD-1⁺ OX40⁺ costimulated CD4 T cells → **better DFS**.
- Δ(D15–D0) → RVT:** ↑ CD115⁺ granulocytes → **lower RVT**; ↑ terminally differentiated/senescent CD28⁺ CD57⁺ CD8 T cells and inflammatory FcγRI/CD64⁺ monocytes → **higher RVT**.
- Overall:** pre-existing activation is unfavourable; treatment-induced activation is favourable when proliferative capacity is preserved.

*RVT = Residual Vital Tumour