Supplementary Figures

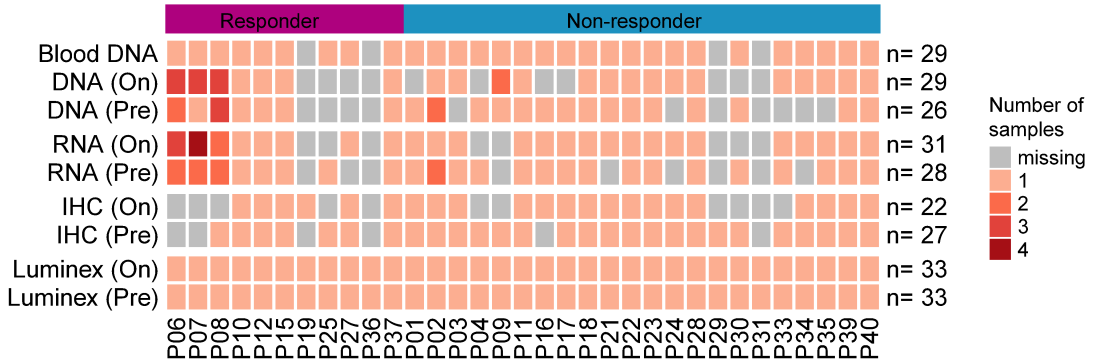

Figure S1: Summary of sample size across different assays. These sample sizes reflect number of samples used in analyses.

Output of logistic regression (Response~TMB+Purity)

	term	estimate	std.error	statistic	p.value
1	(Intercept)	3.0666582	2.0090521	1.5264205	0.12690518
2	TMB	−0.9857306	0.4863127	−2.0269480	**0.04266773**
3	Purity	1.7464890	2.1432223	0.8148894	0.41513565

Figure S2: Output of multivariate logistic regression when predicting Response. Purity of samples were included as covariate in the model to rule out the effect of tumor purity differences in TMB of samples.

Kaya NA, *et al. J Immunother Cancer* 2023; 11:e007106. doi: 10.1136/jitc-2023-007106

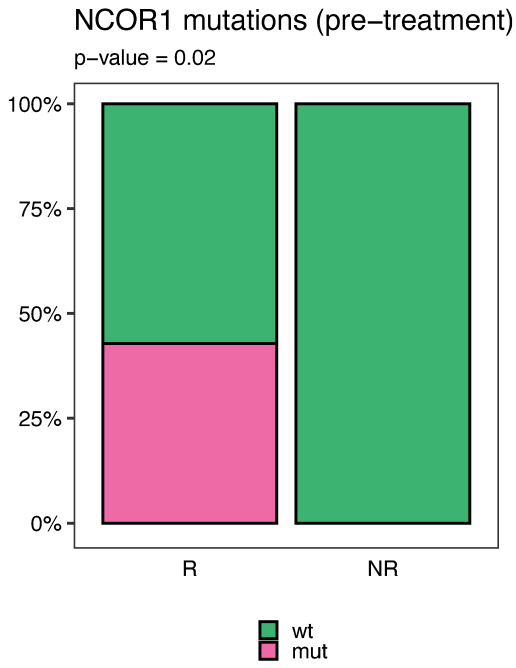

Figure S3: Percentage of NCOR1 mutations in responders and non-responders at the baseline (pre-treatment). Three out of seven responders have NCOR1 mutations while none of the 15 non-responders have baseline mutations in this gene.

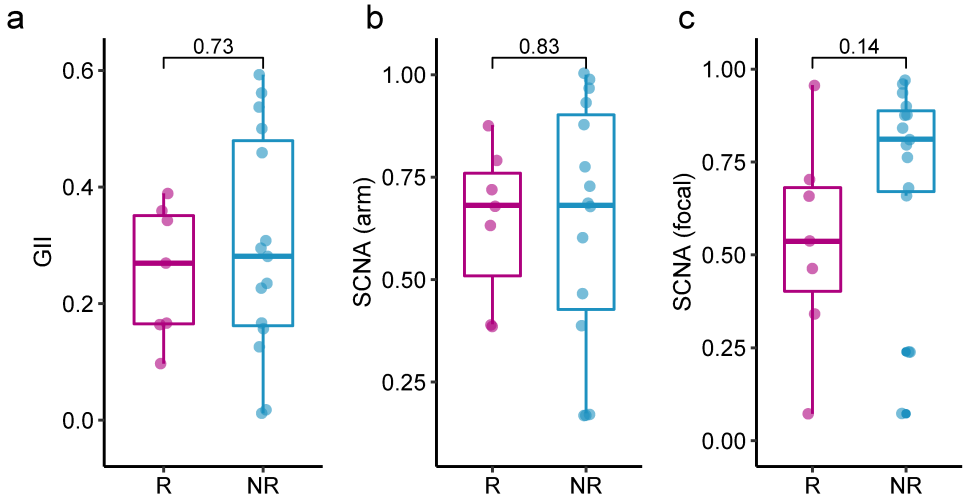

Figure S4: Comparison of copy number burden using a) Genomic instability index (GII) b) Arm-level somatic copy number alteration score (SCNA arm) c) Focal-level somatic copy number alteration score (SCNA focal)

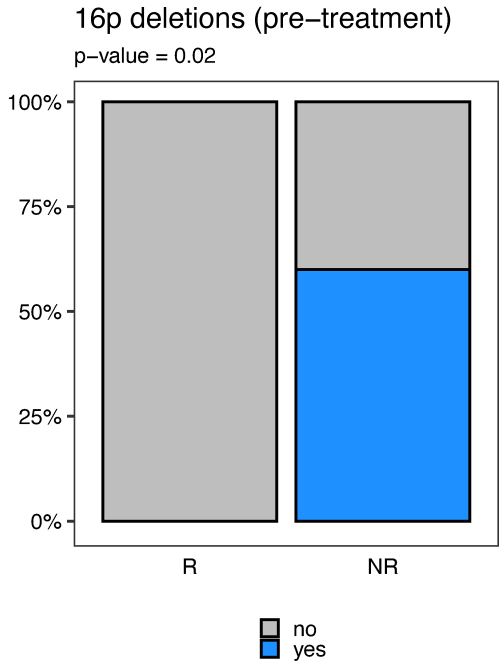

Figure S5: Percentage of 16p arm deletions in responders and non-responders at the baseline (pre-treatment). While responders (n=7) did not have deletion in chromosome 16p, 9 out of 15 non-responders had deletions in this chromosome arm.

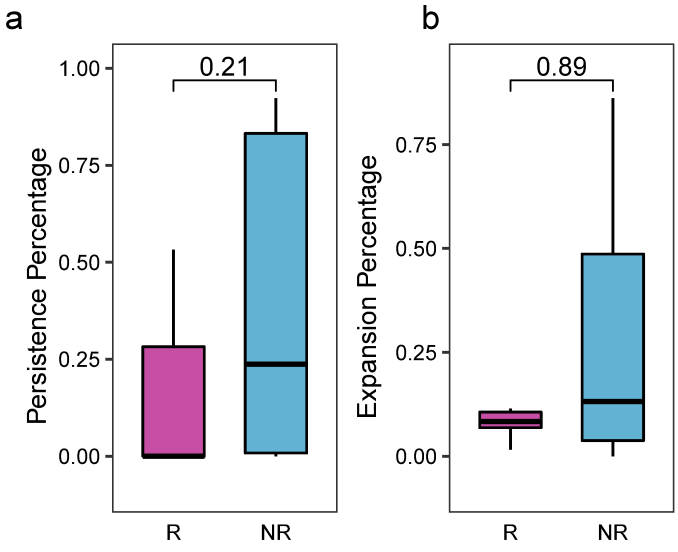

Figure S6: Comparison of a) persistent and b) expanding mutation percentage between R and NR

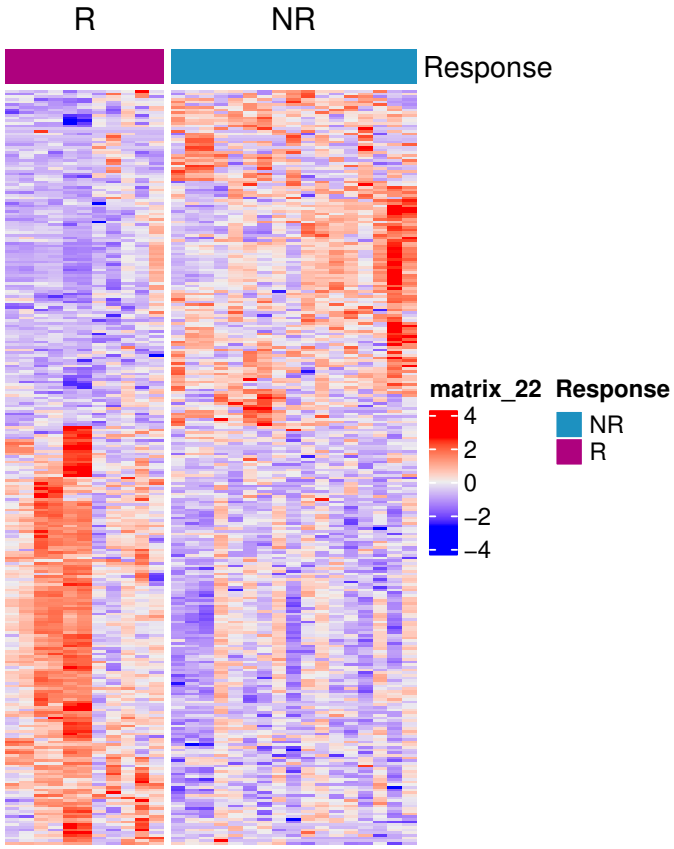

Figure S7: Normalized gene expression heatmap for differentially expressed genes between R and NR

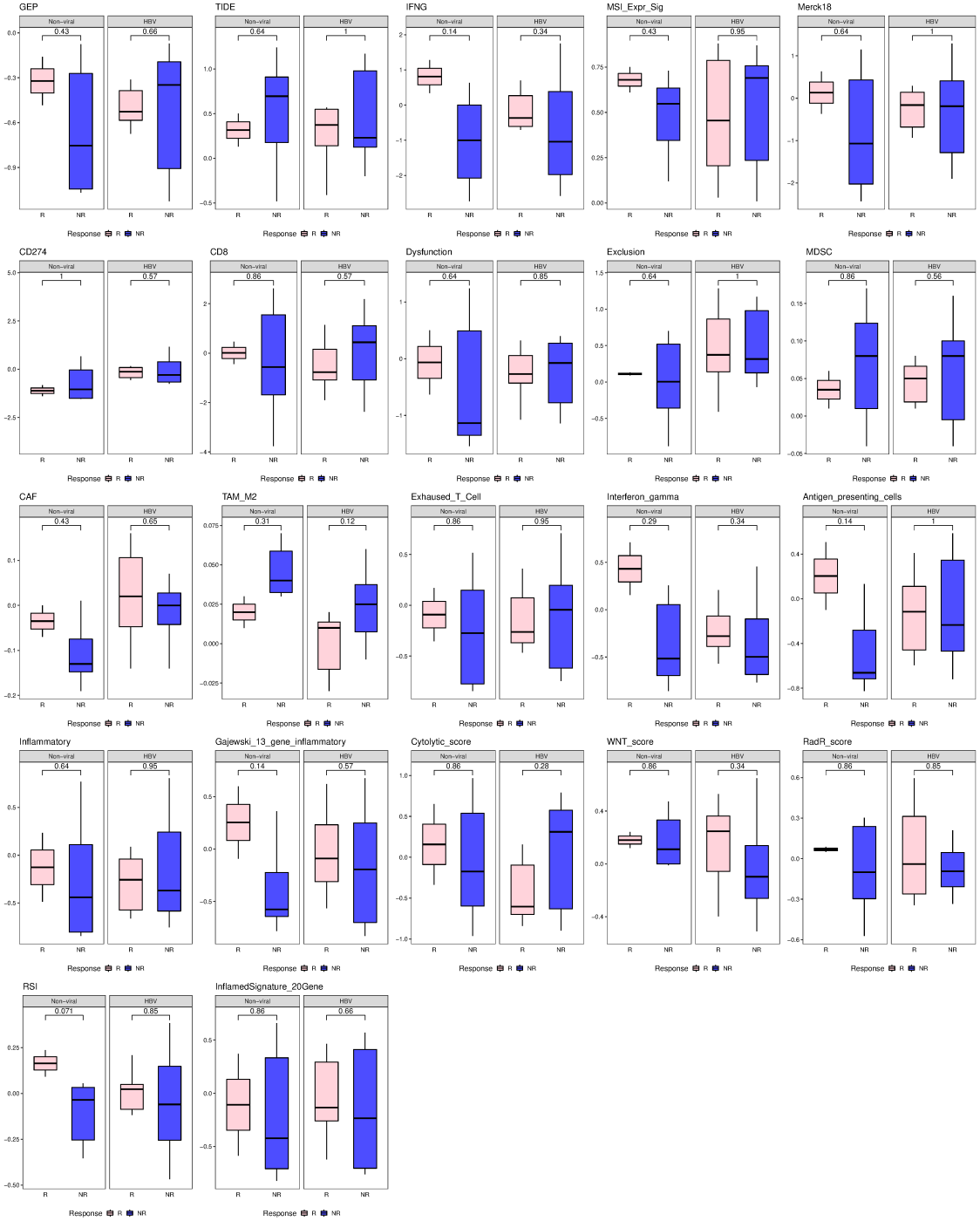

Figure S8: Comparison of baseline levels of 22 previously reported biomarkers stratified by viral status.

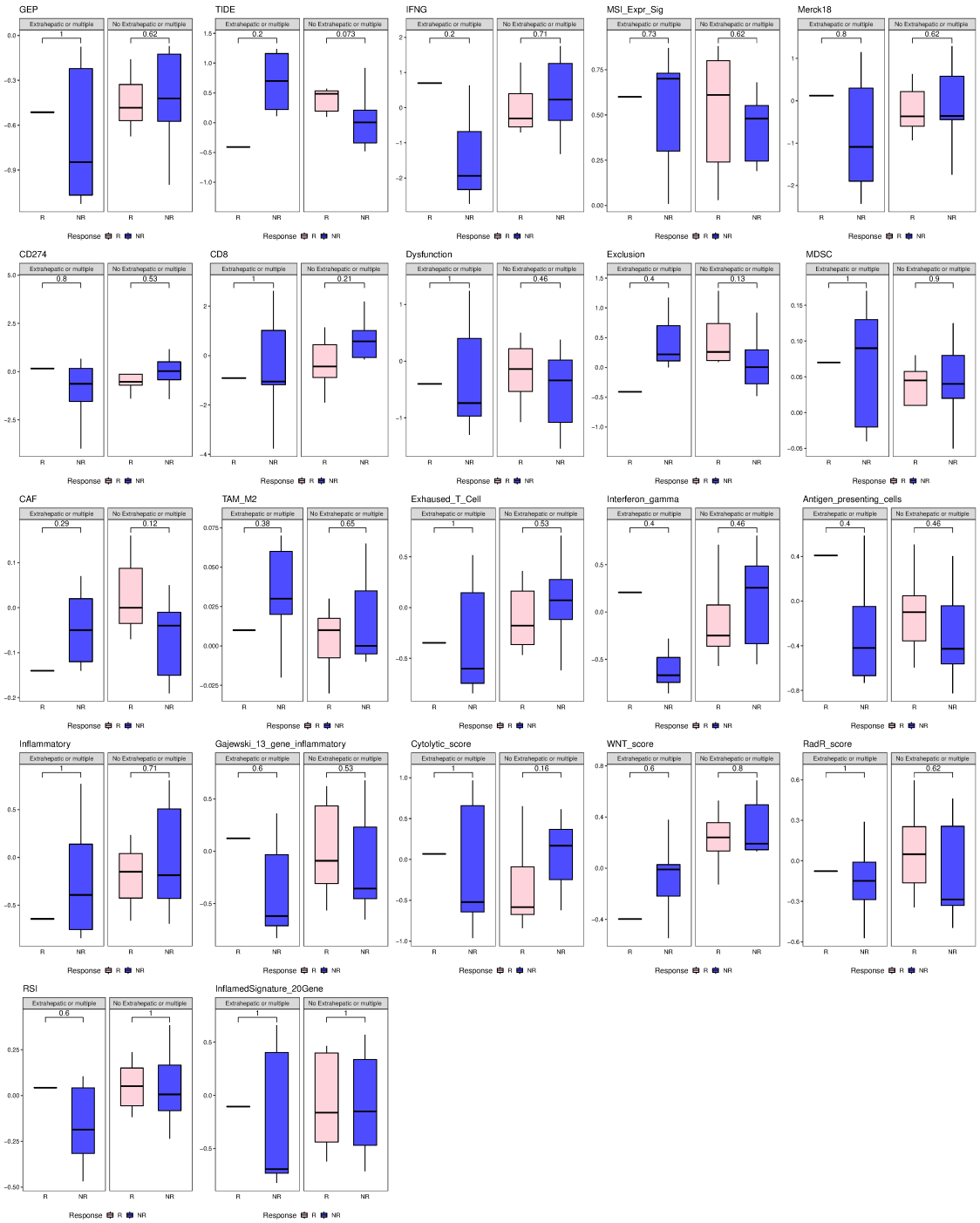

Figure S9: Comparison of baseline levels of 22 previously reported biomarkers in patients without extrahepatic spread or multiple liver lesions (N) and patients with extrahepatic spread and/or multiple liver lesions (Y)

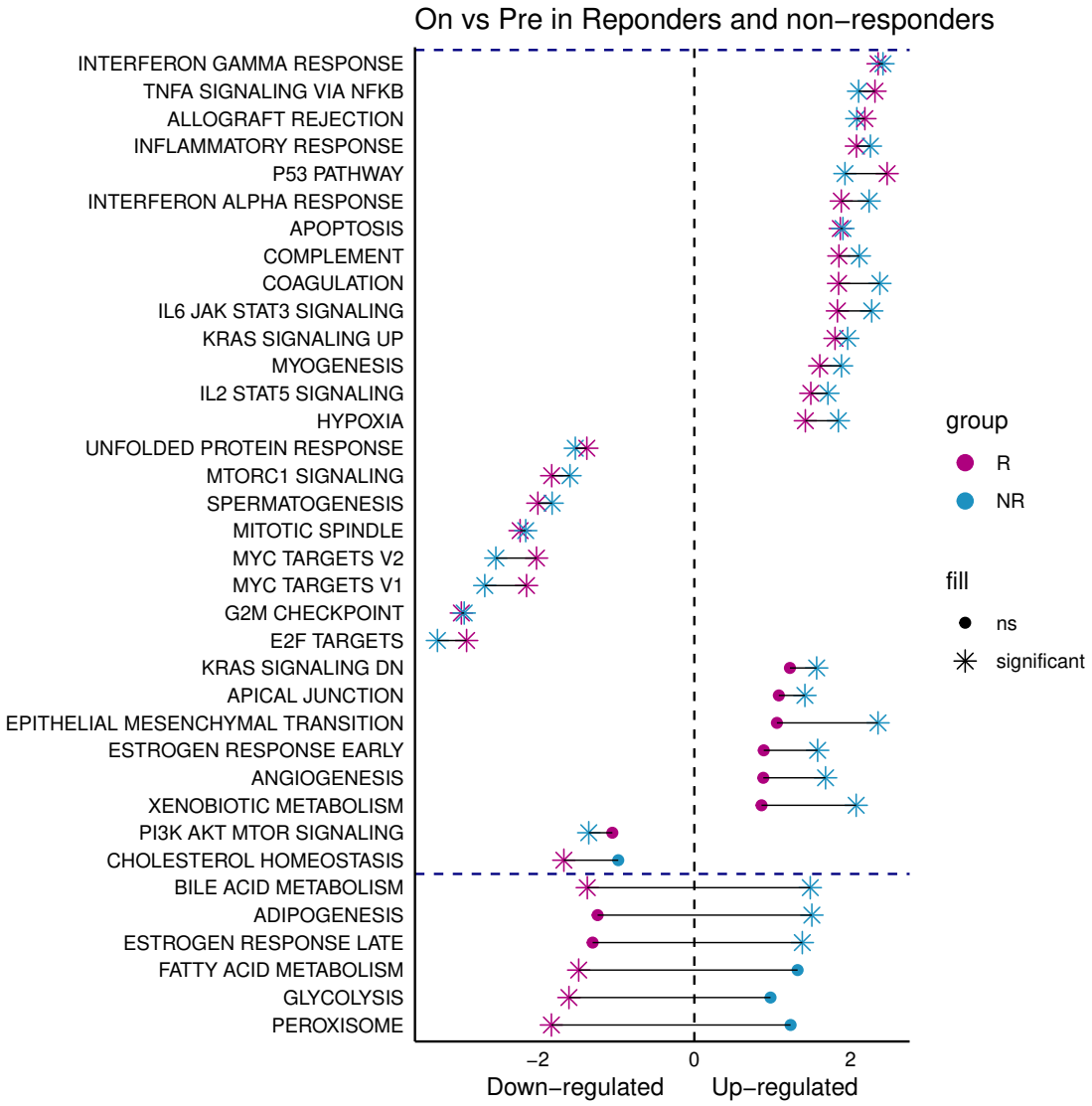

Figure S10: The complete version of enriched pathways in R and NR when comparing baseline and on-treatment samples. Stars indiate a significant enrichment (fdr < 0.05). While majority of significant pathways showed similar direction in both R and NR, metabolism related pathways such as bile acid metabolism were changed in opposite direction in R and NR.

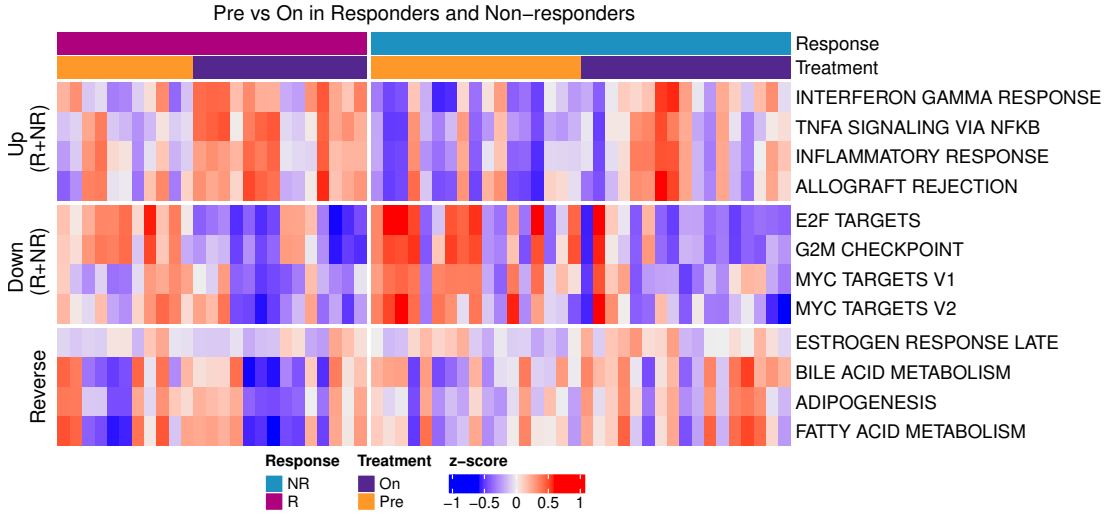

Figure S11: Gene set variation analysis (GSVA) scores of pathways associated with treatment response. Example pathways from pathways changing in the same direction (Up and Down) as well as the opposite direction (Reverse) are shown.

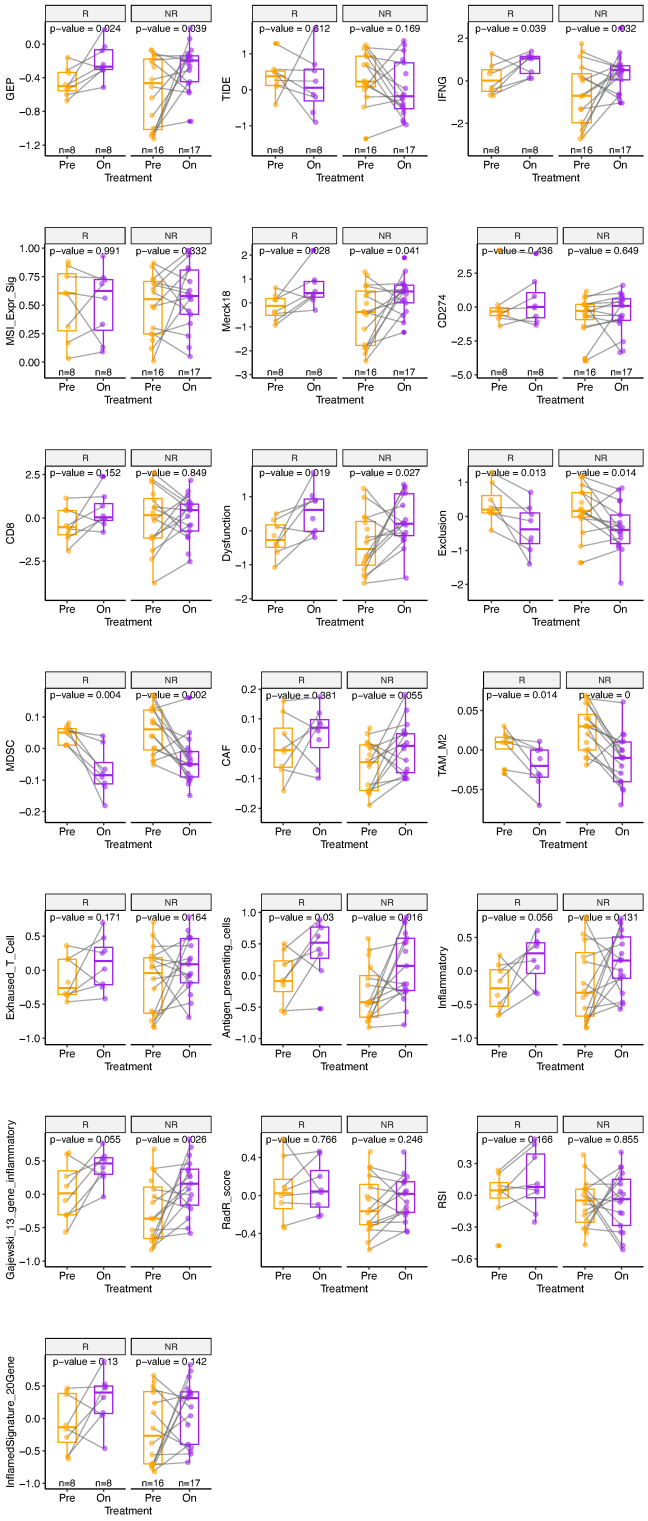

Figure S12: Boxplots for reported ICB response signatures (n=19).In total 22 signatures are examined and three of them are shown in Figure 4.

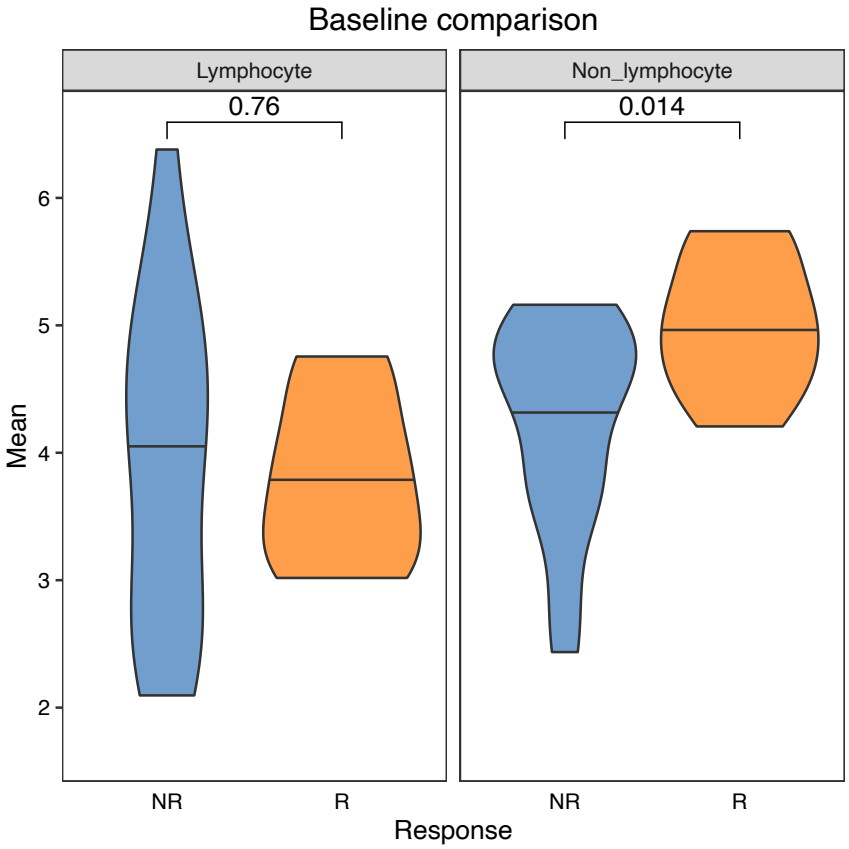

Figure S13: Comparison of lymphocyte and non-lymphocyte Danaher cell scores between R and NR. Non-lymphocyte score is calculated as the average Danaher scores of DC, macrophages, mast cells and neutrophils.

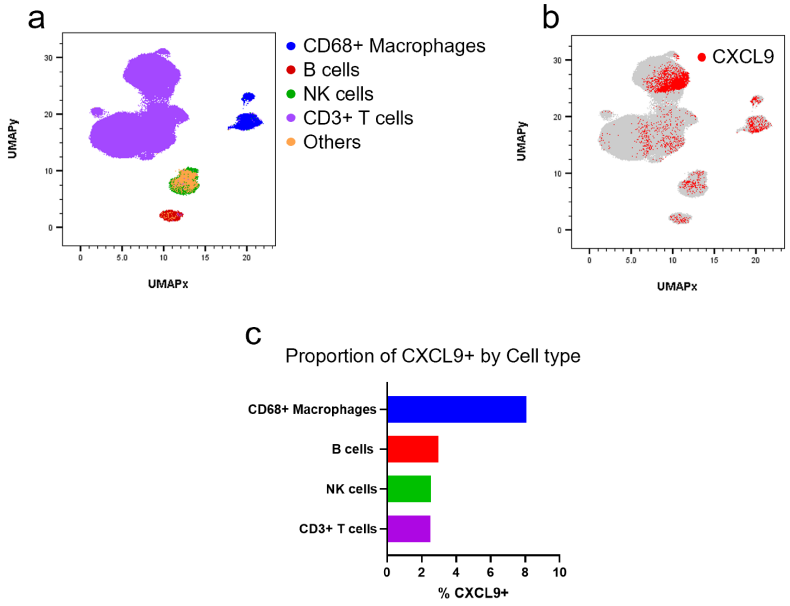

Figure S14: Unsupervised analyses of PBMCs showed CXCL9+ cells are largely macrophages. a) Representative UMAP plot for visualisation of the clustering of major cell lineages from all live immune cells. Major cell lineages are indicated by colours. b) Visualisation of CXCL9+ cells expression on the representative UMAP plot. Majority of the CXCL9+ cells were shown to be expressed on the CD68+ macrophages cluster. c) Bar chart showing the proportion of CXCL9+ cells for each cell type. CD68+ macrophages lineage has the most proportion of CXCL9+ cells.

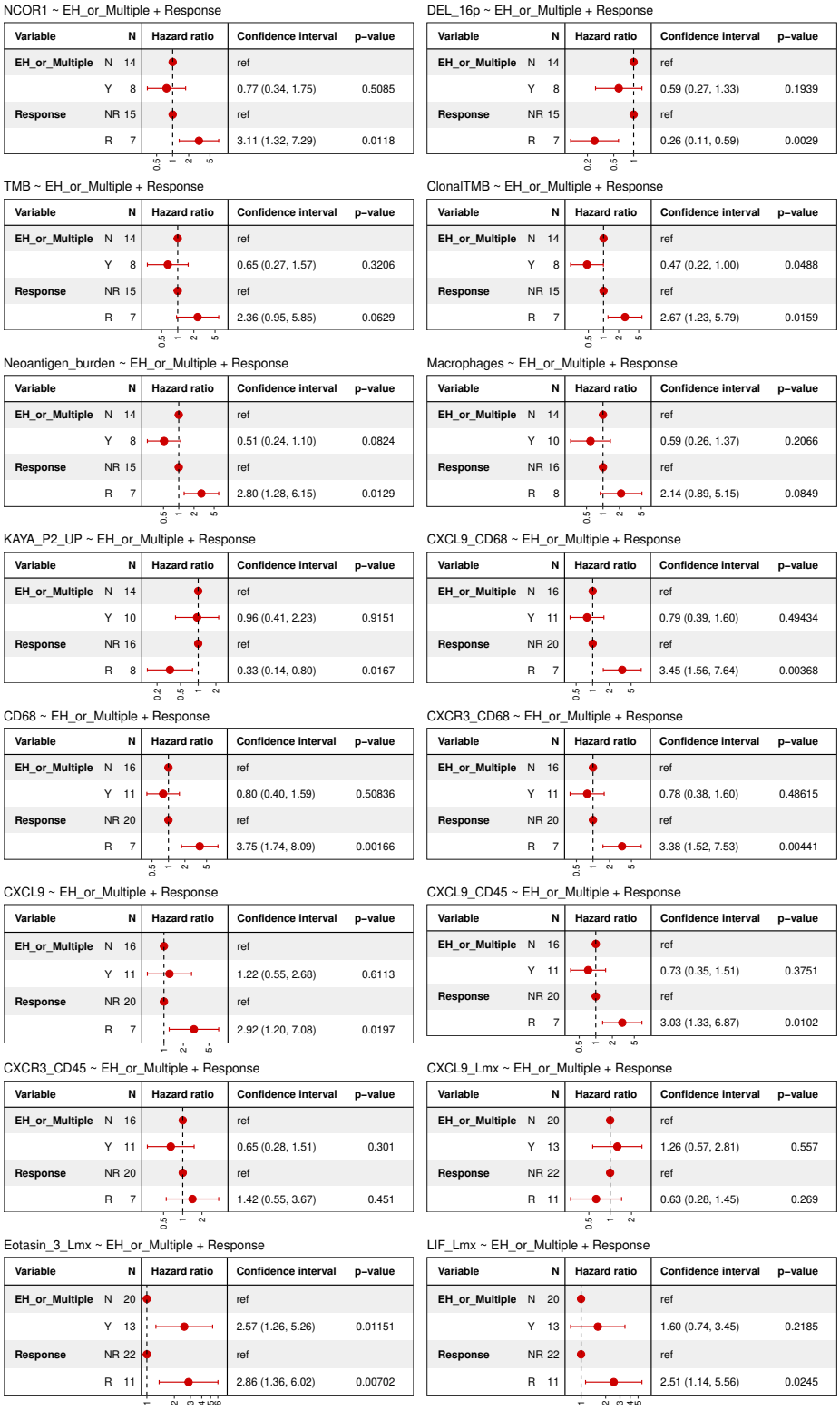

Figure S15: Linear regression models for our findings to account for extrahepatic spread and multiple liver tumors. While mostly extrahepatic spread or multiple liver lesion variable is not significantly associated with the biomarker, response variable remains significant.

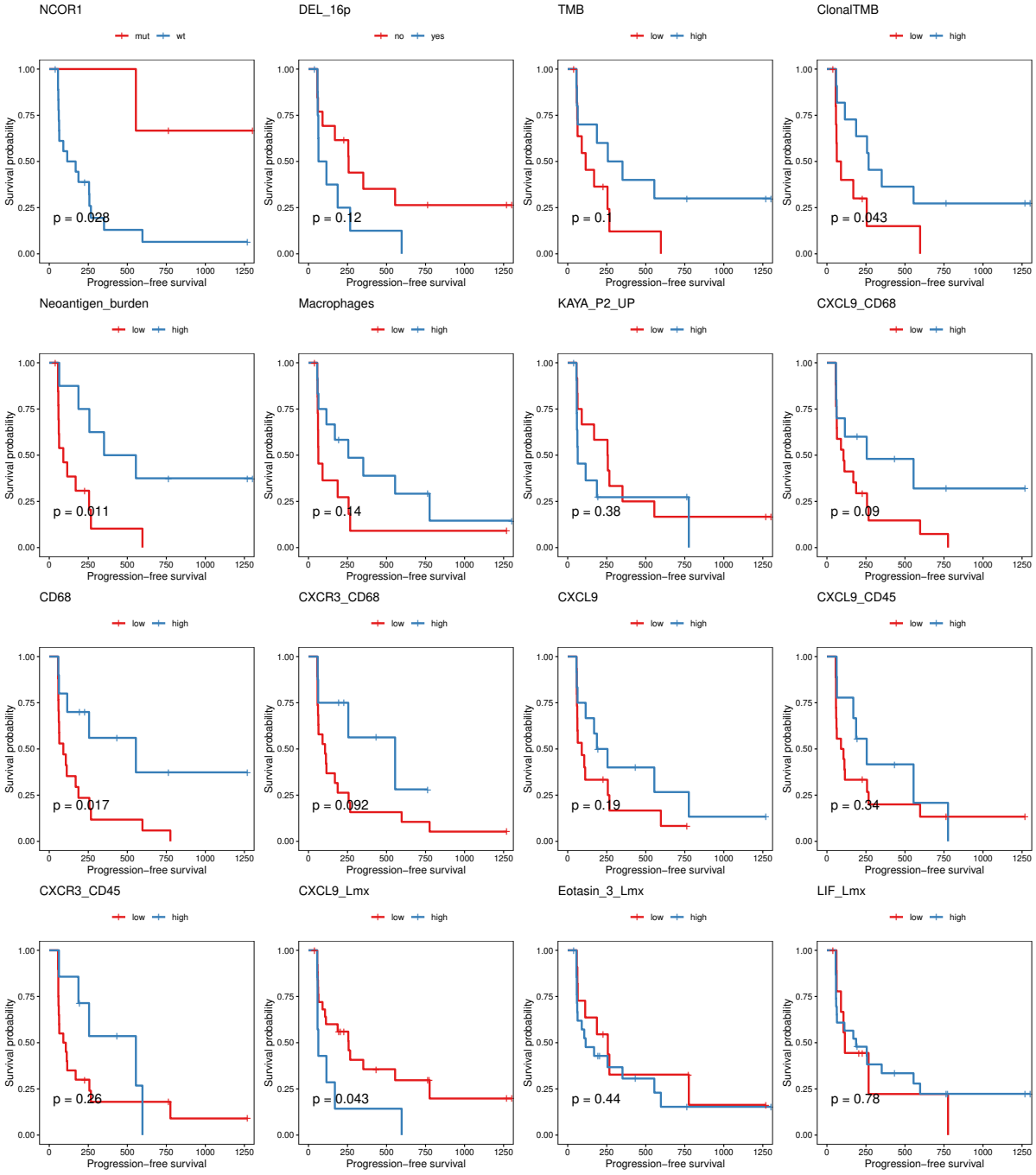

Figure S16: Kaplan Meier plots using progression-free survival for significant biomarkers (n=16). Continious variables were categorized as high and low based on the mean value across all patients.

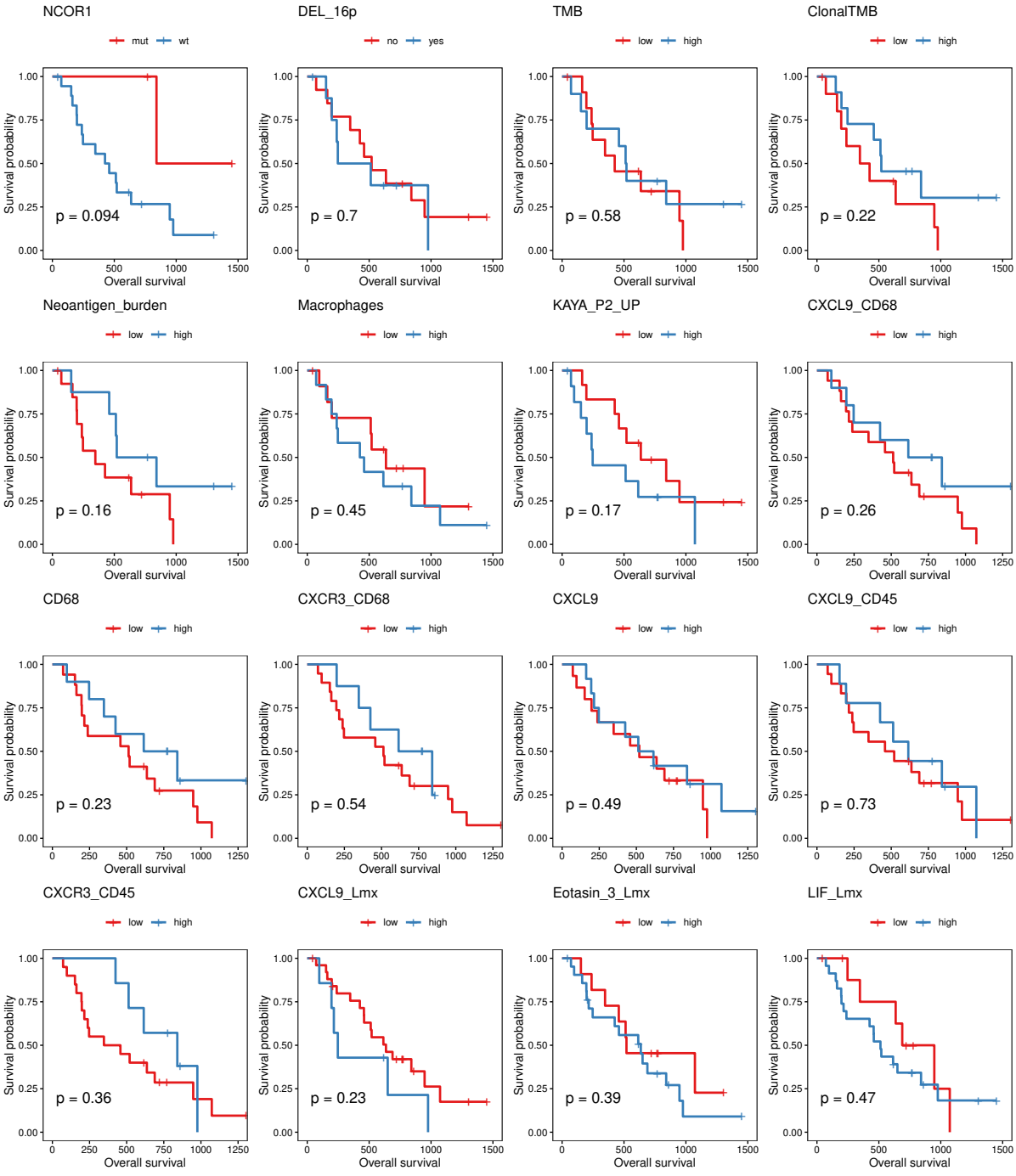

Figure S17: Kaplan Meier plots using overall survival for significant biomarkers (n=16). Continious variables were categorized as high and low based on the mean value across all patients.

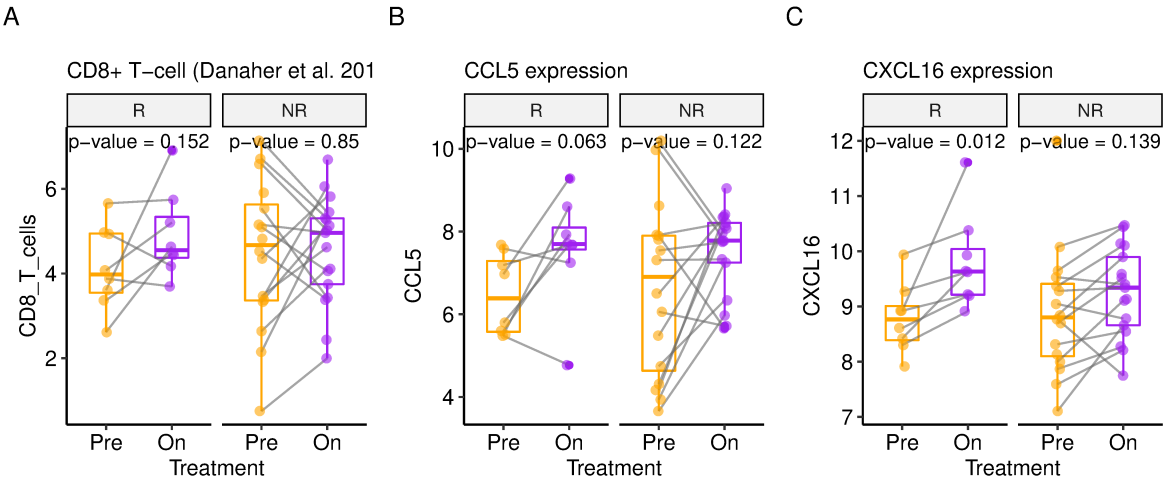

Figure S18: Dynamic changes in CD8+ Tcells, CCL5 and CXCL16 gene expressions in Responders and Nonresponders