

Supplementary Materials

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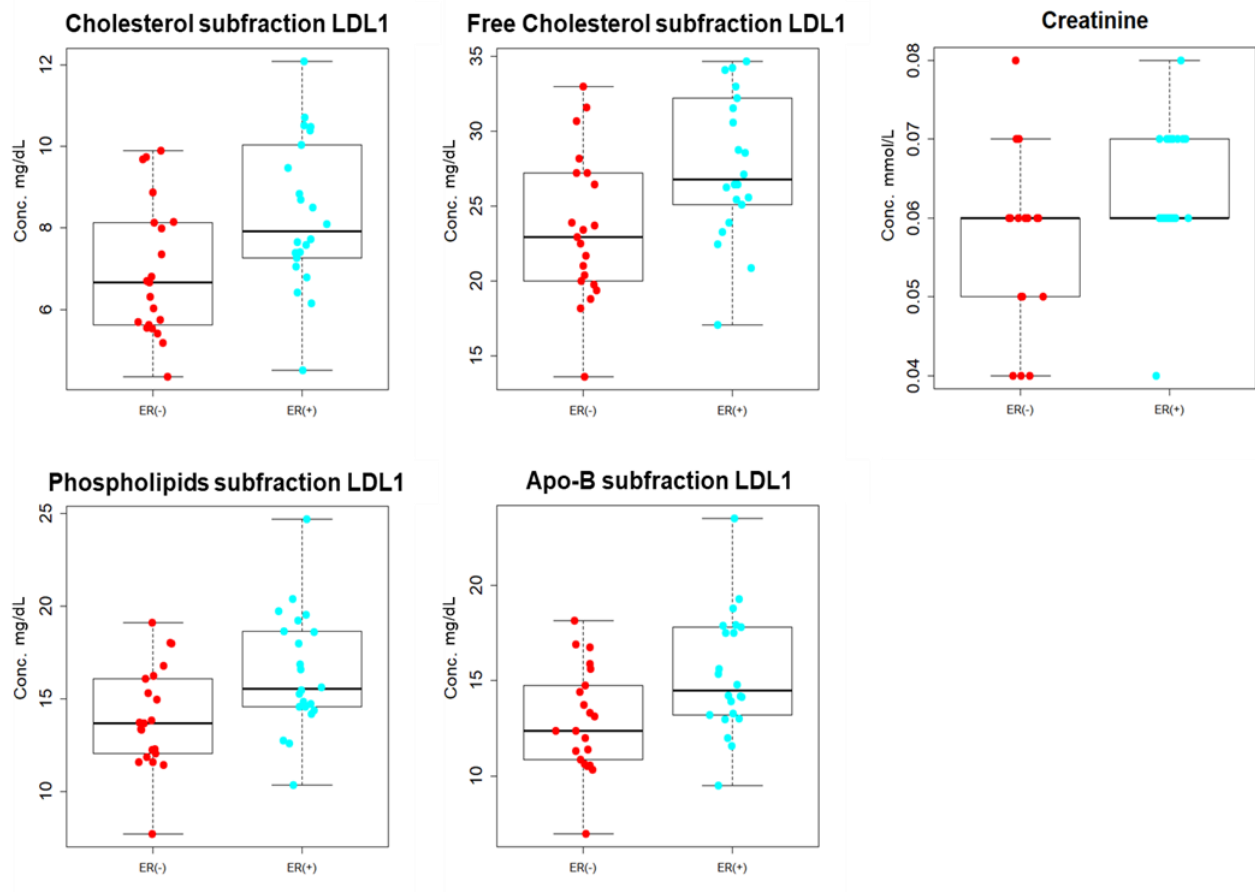


Figure S1. Comparison between ER(-) and ER(+) BC patients on baseline plasma samples via ¹H NMR metabolomics. Metabolites and lipid fractions that significantly contribute to the discrimination are reported.

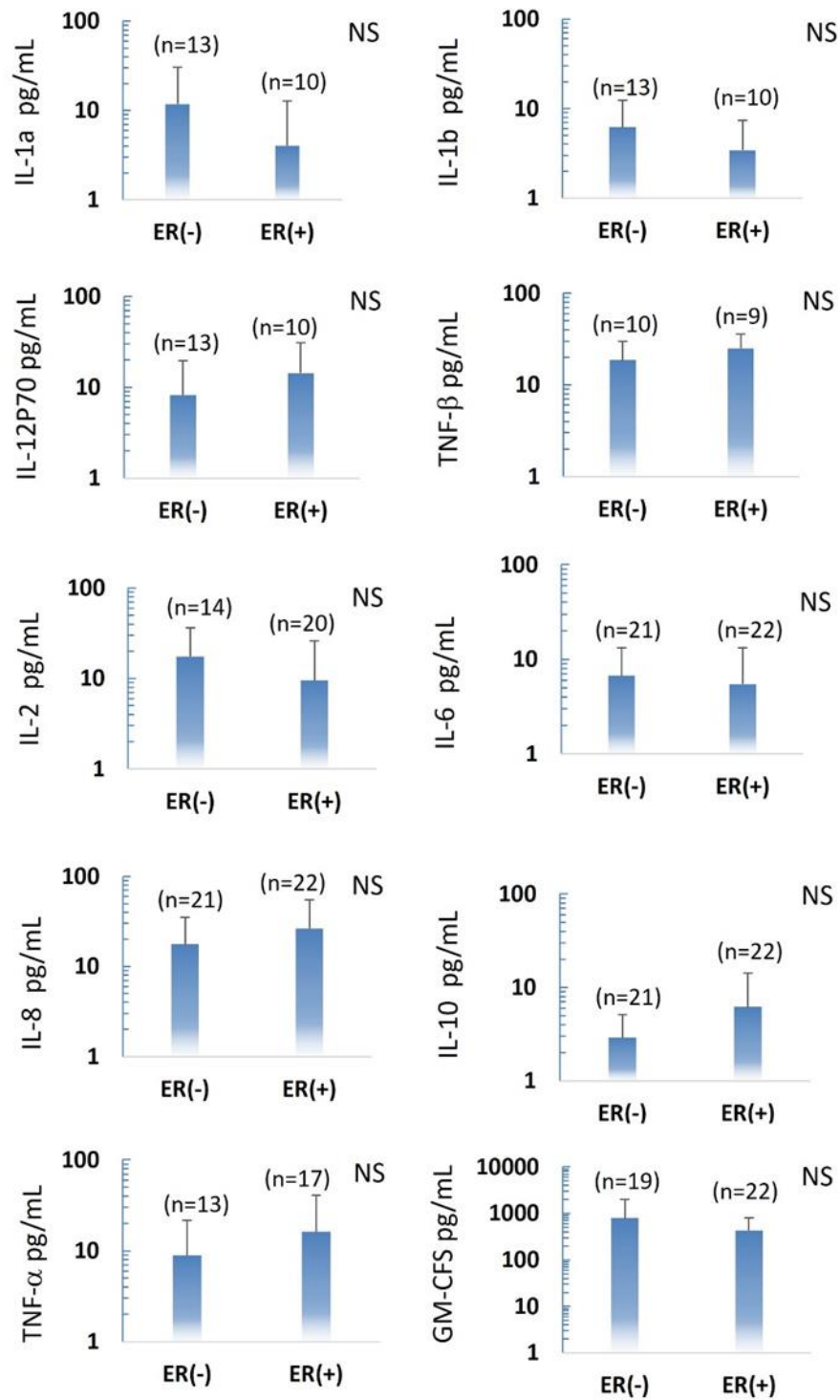


Figure S2. Concentration of 10 cytokines in the serum HER2-positive ER(+) and ER(-) BC patients. Mean + Standard Deviation (SD). n: number of patients for which each cytokine was quantify reported parenthesis. NS: No statistical significative.

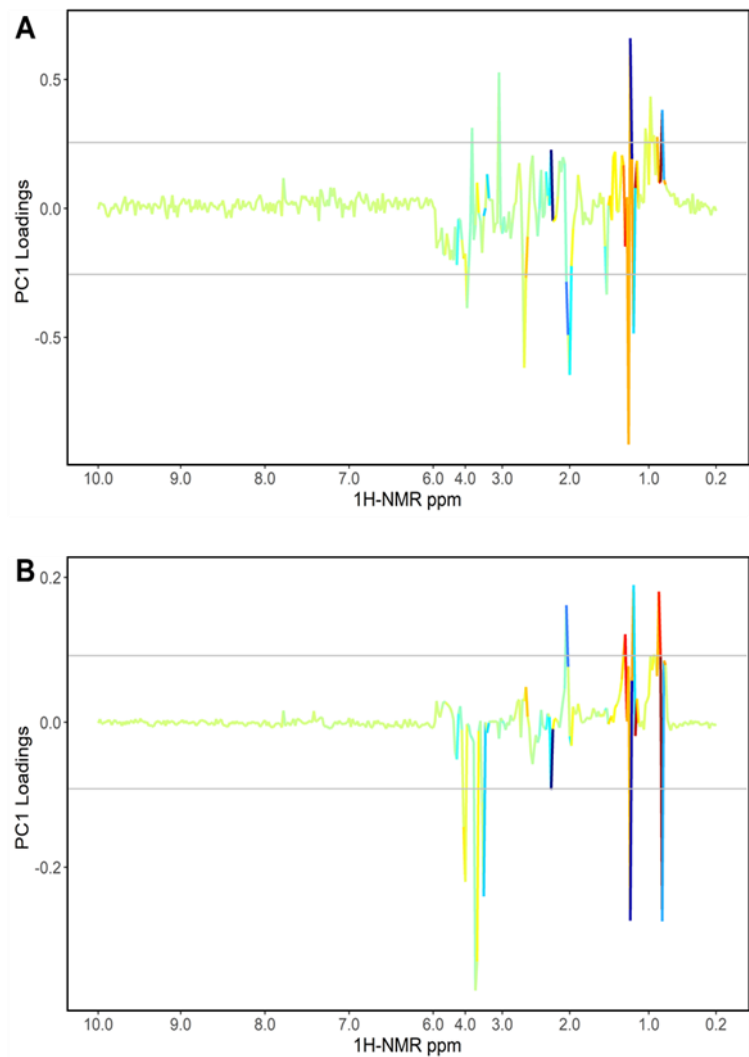


Figure S3. Analysis of baseline plasma samples via ^1H NMR metabolomics to compare GR and PR patients to NATC in ER(+) (A) and ER(-) (B) patients; Loading plots of the first component of the PCA-CA calculated on the CPMG spectra.

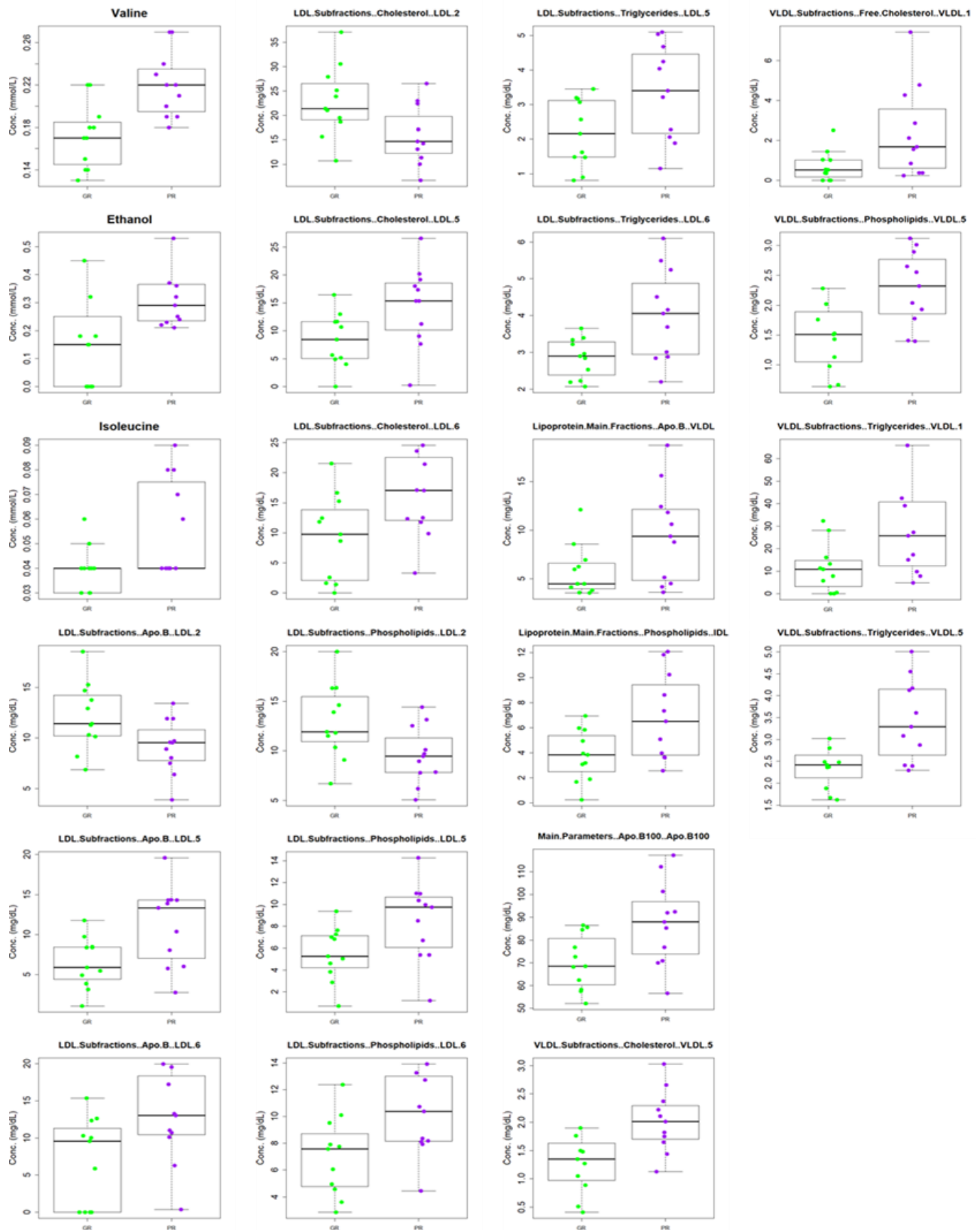


Figure S4. Comparison between GR and PR ER(+) patients at baseline via ^1H NMR metabolomics. Metabolites and lipid fractions that significantly contribute to the discrimination are reported.

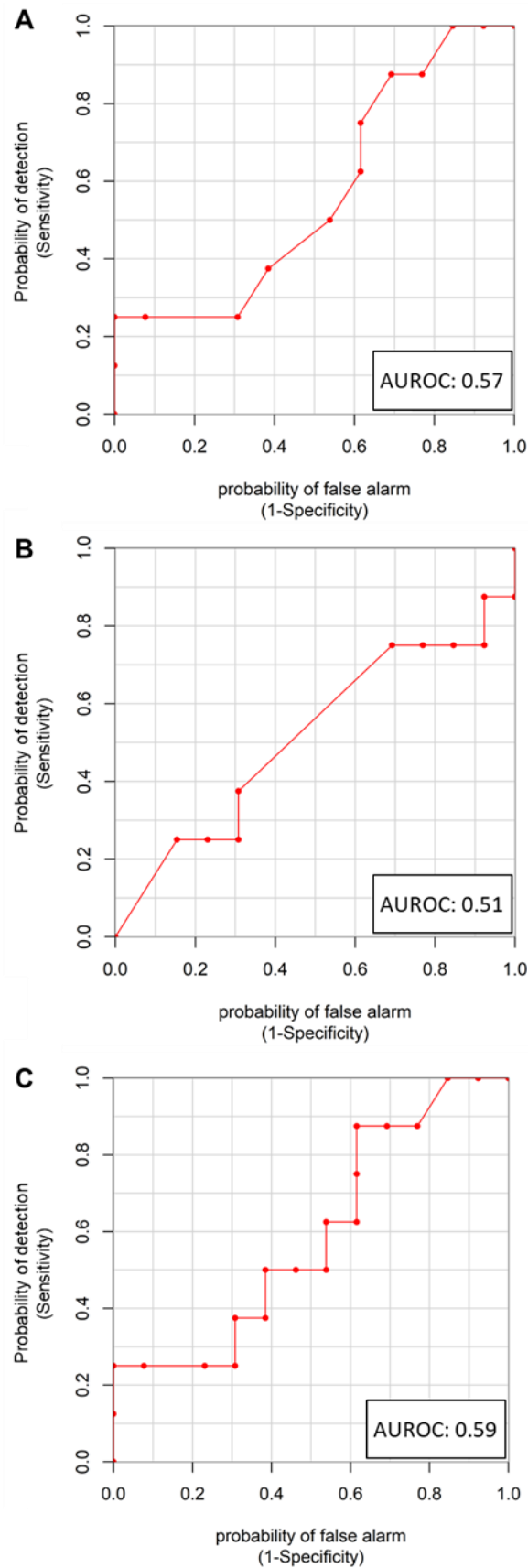


Figure S5. ROC curves of valine (A) and TNF- α (B) diagnostic power to distinguish ER(-) patients who achieve pathological response (GR) from those who achieve only a partial response (PR) to NATC treatment. The ROC curve of the combined linear model VAL+TNF- α (C) shows improved (not relevant) diagnostic power.

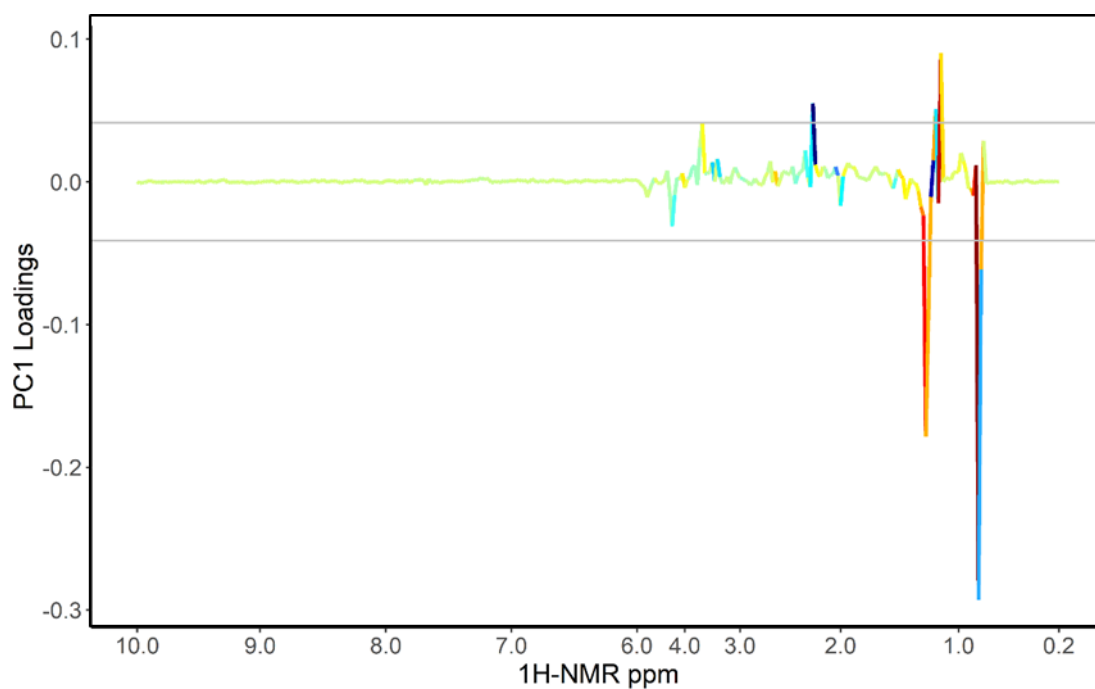


Figure S6. Baseline ^1H NMR metabolomic profile comparison between ER(+) patients who developed disease recurrence and those who were disease free at 10 years. Loading plots of the first component of the PCA-CA calculated on the CPMG spectra.

Table S1. Analysis of cytokines in ER(+) patients to discriminate the patients who achieve pathological response (GR) from those who achieve only a partial response (PR) to NATC treatment.

	AUROC	P-value	P-value adjusted with FDR	Cliff's delta effect size
IL-2	0.70	0.12	0.37	0.40
IL-6	0.52	0.90	0.90	0.04
IL-8	0.64	0.29	0.50	-0.27
IL-10	0.53	0.85	0.90	-0.06
TNF-α	0.84	0.01	0.04	0.68
GM-CSF	0.62	0.33	0.50	0.23

Table S2. Analysis of cytokines in ER(-) patients to discriminate the patients who achieve pathological response (GR) from those who achieve only a partial response (PR) to NATC treatment.

	AUROC	P-value	P-value adjusted with FDR	Cliff's delta effect size
IL-2	0.58	0.58	0.70	-0.15
IL-6	0.61	0.46	0.68	-0.21
IL-8	0.79	0.03	0.15	0.58
IL-10	0.74	0.08	0.15	0.48
TNF-α	0.51	0.94	0.94	0.03
GM-CSF	0.73	0.07	0.15	-0.46

Table S3. Analysis of cytokines in ER(+) patients to discriminate the patients who free from disease and relapsed patients.

	AUROC	P-value	P-value adjusted with FDR	Cliff's deltaeffect size
IL-2	0.77	0.04	0.12	-0.54
IL-6	0.63	0.32	0.48	-0.27
IL-8	0.50	1.00	1.00	-0.01
IL-10	0.79	0.03	0.12	-0.57
TNF-α	0.56	0.65	0.79	-0.13
GM-CSF	0.69	0.12	0.23	0.38