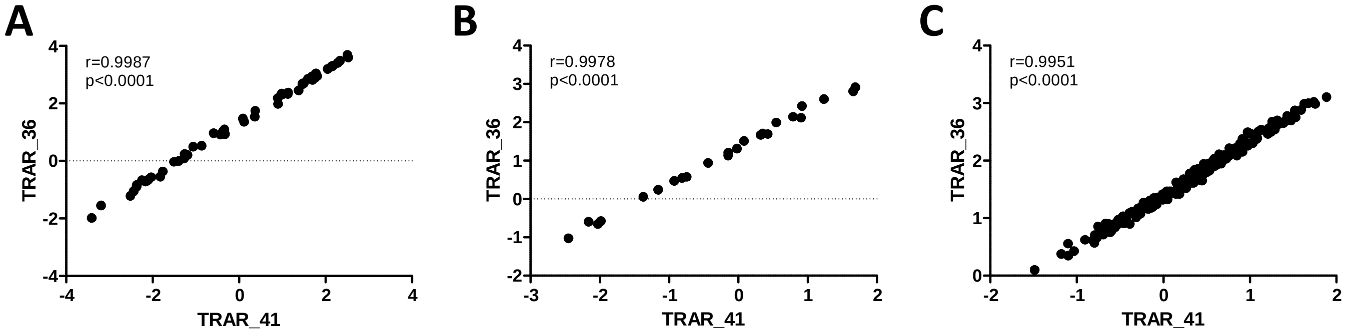
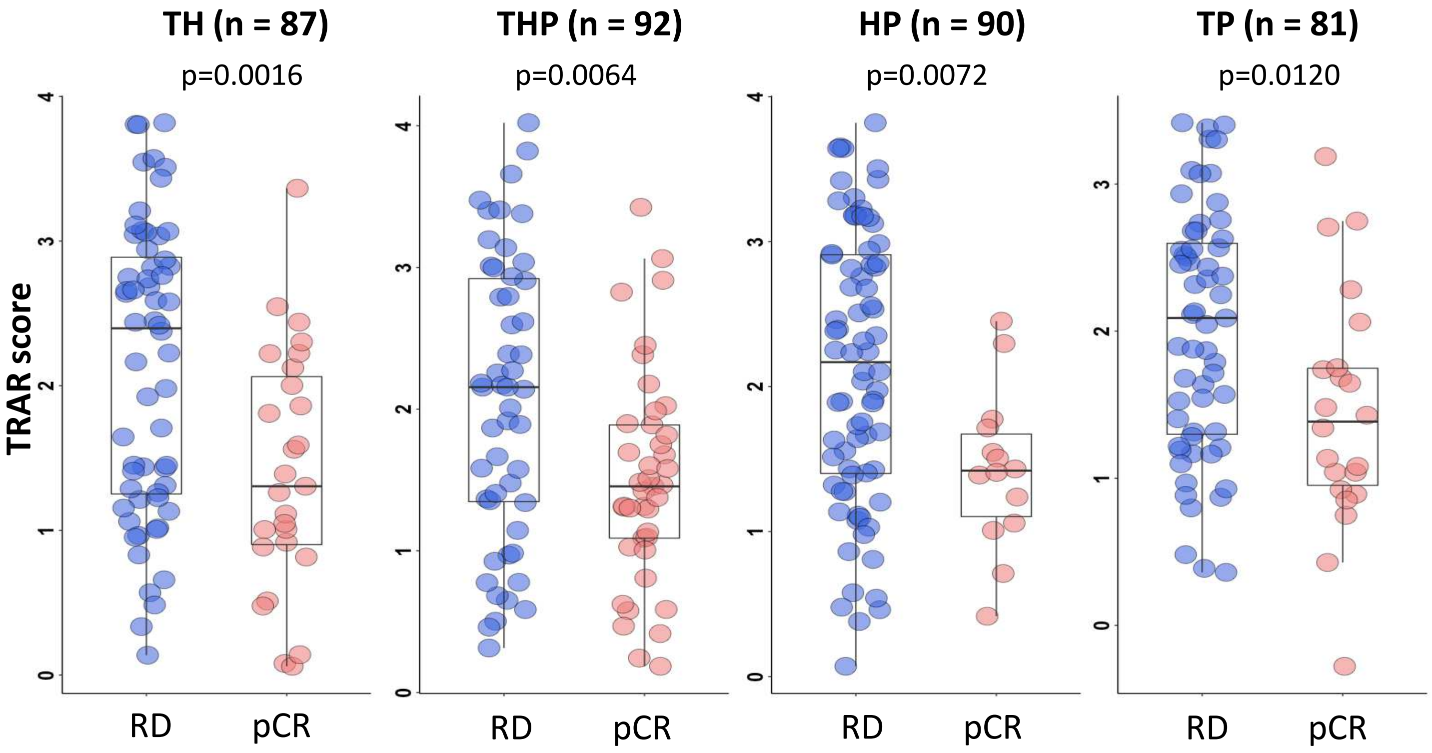
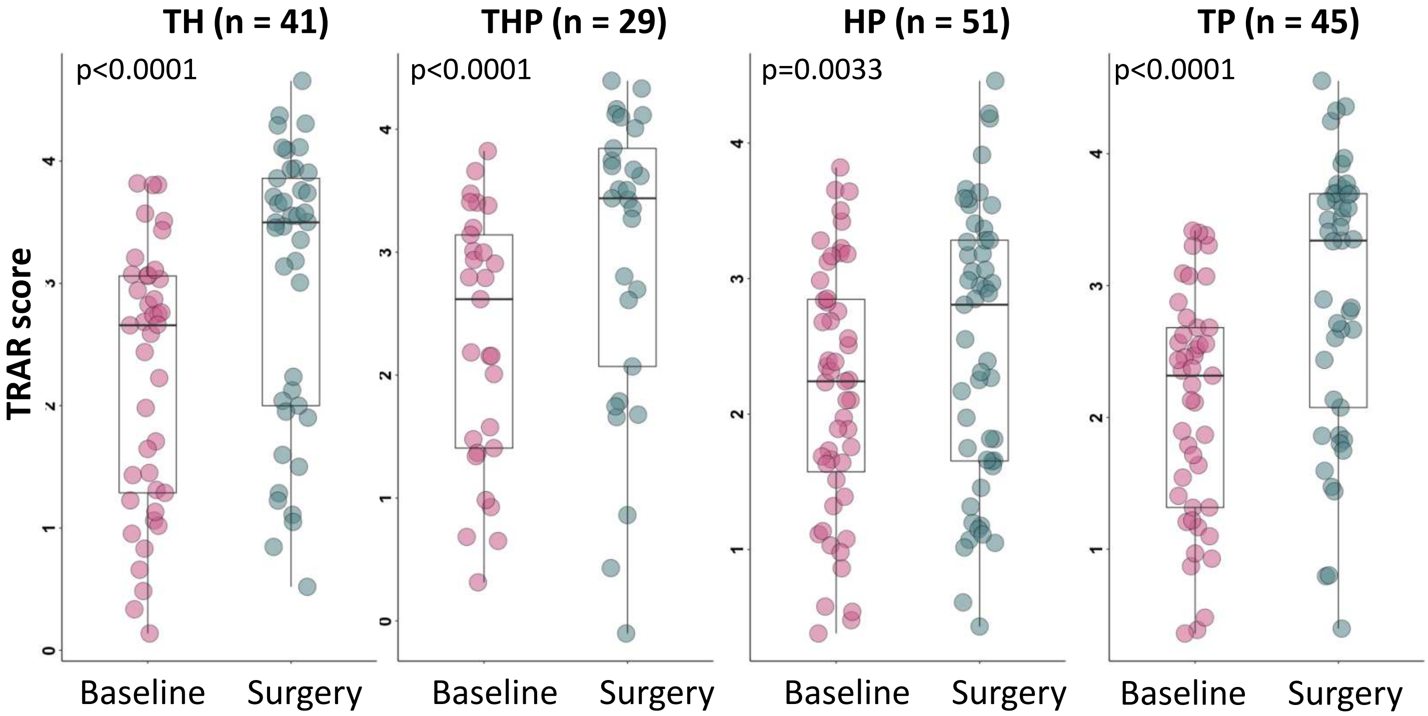


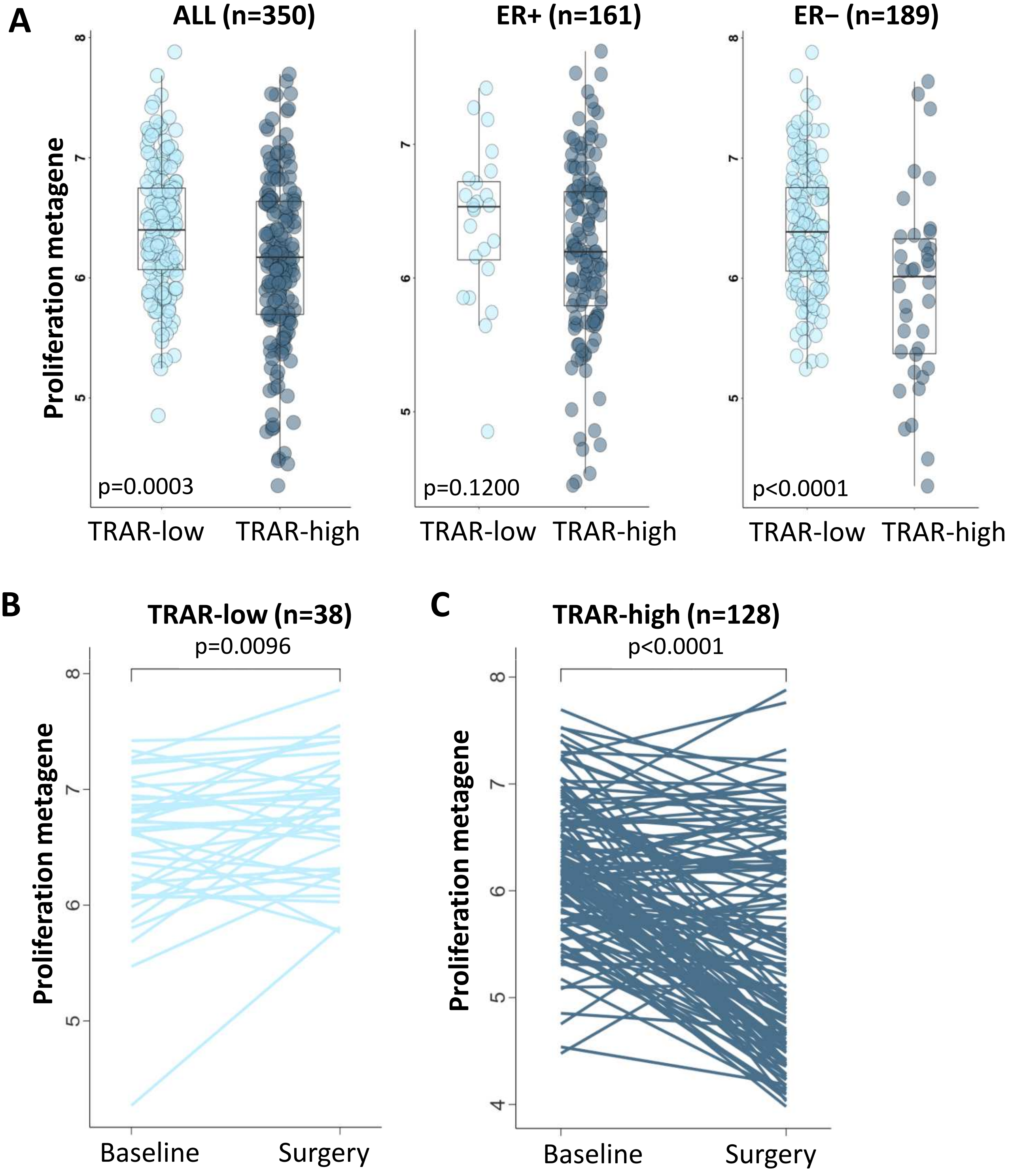
Supplementary Figure 1. TRAR scores according to signature composition. Correlation between TRAR_41 (computed using all genes of the signature) and TRAR_36 (computed using 36 genes of the signature as done in the NeoSphere cohort) in GHEA (A, n=54), TRUP (B, n=24) and NeoALTTO (C, n=226) datasets. r, Pearson correlation coefficients and related p-values are shown.



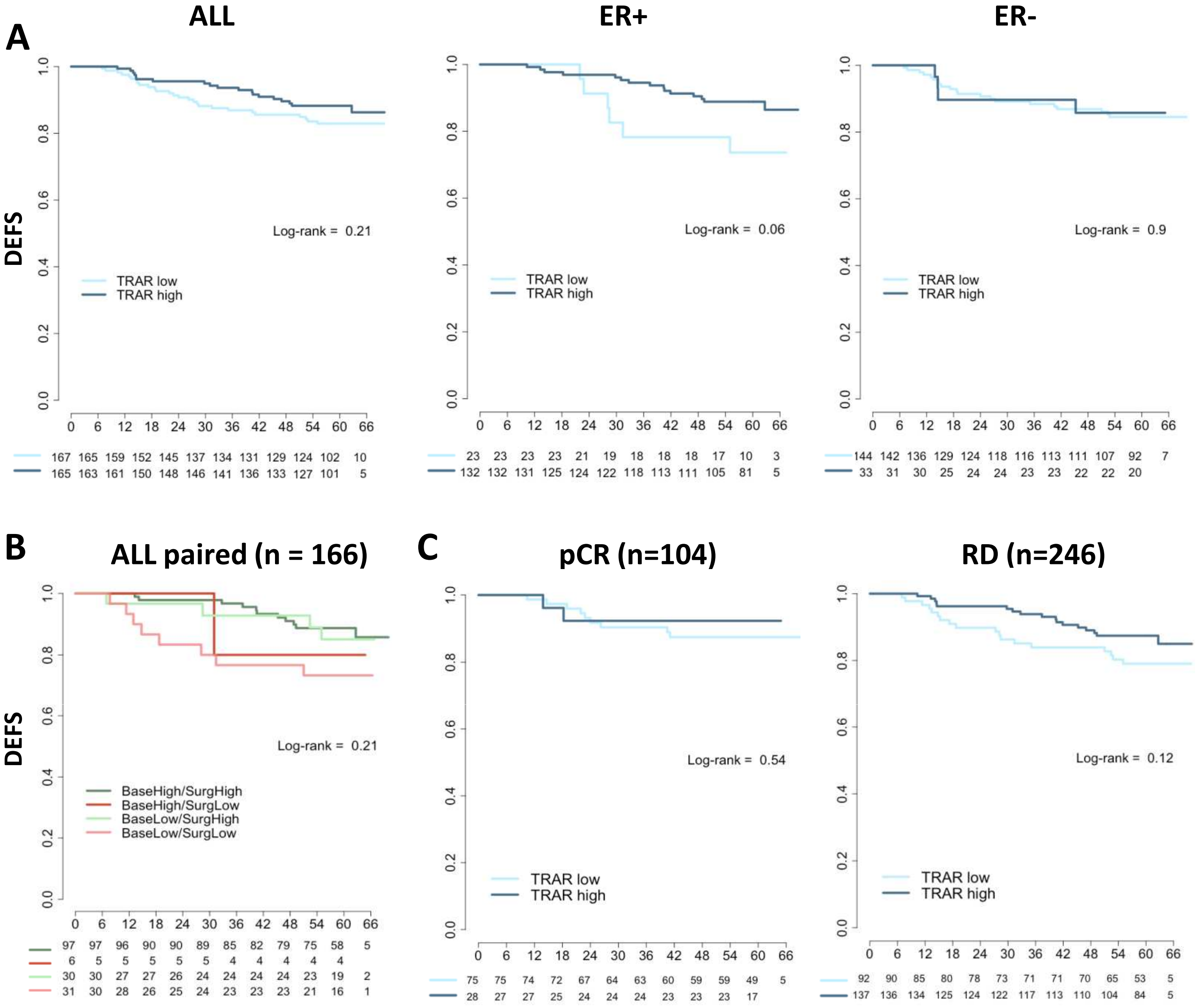
Supplementary Figure 2. Predictive performance of TRAR according to treatment arm. Box-plots of the distribution of TRAR score in patients with residual disease (RD) and pathological complete response (pCR) in each Neosphere treatment arm. p-values by Wilcoxon test. T, taxane; H, trastuzumab; P, pertuzumab.



Supplementary Figure 3. TRAR modulation according to treatment arm. Box-plots of the distribution of TRAR score as evaluated in pre-treatment biopsies (Baseline) and at surgery of patients enrolled in each Neosphere treatment arm. p-values by Wilcoxon test. T: taxane, H: trastuzumab, P: pertuzumab.



Supplementary Figure 4. Proliferation metagene according to TRAR. Box-plots of the distribution of proliferation metagene expression in TRAR-low and TRAR-high tumors at baseline in the overall cohort (n=350), in ER+ (n=161) and ER− (n=189) subgroups. p-values by Wilcoxon test. B-C) Spaghetti plots of the change in proliferation metagene between basal biopsies (Baseline) and samples at surgery in TRAR-low (n=38, B) and TRAR-high (n=128, C) tumors. p-values by paired Wilcoxon test.



Supplementary Figure 5. Prognostic performance of TRAR. A) Kaplan-Meier estimates of distant event-free survival (DEFS) according to TRAR in the pre-treatment cohorts. B) Kaplan-Meier estimates of DEFS in 166 matched cases according to modulation of TRAR. C) Kaplan-Meier estimates of DEFS according to TRAR in patients of the pre-treatment cohort who achieved pCR (pCR) or not (RD). p-values by Log-Rank test.