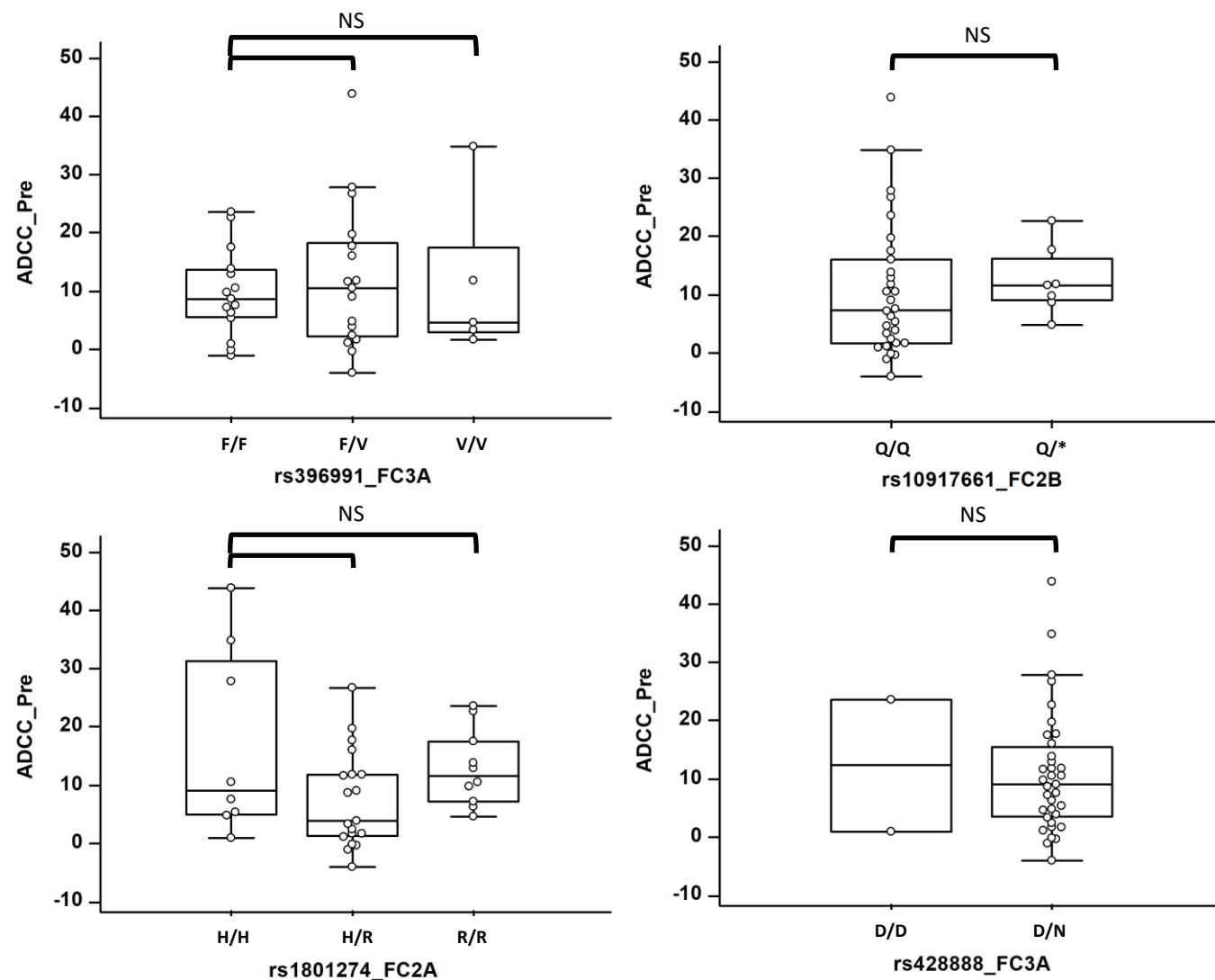


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Supplementary Table 1
and Supplementary
Figures 1-8**

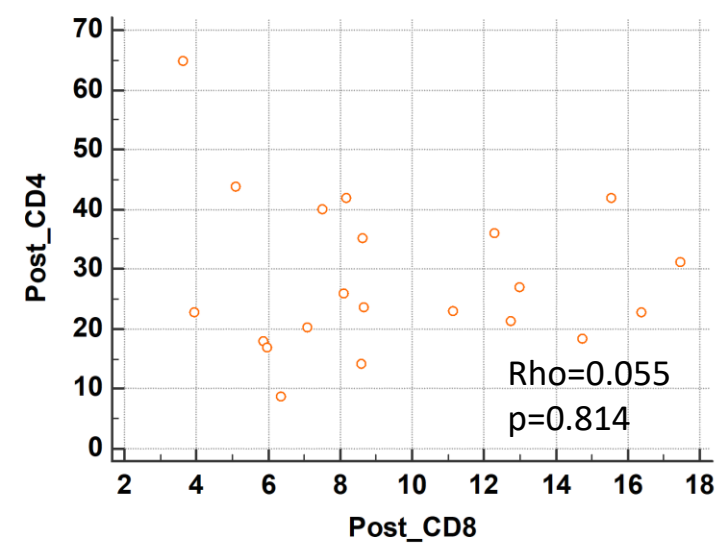
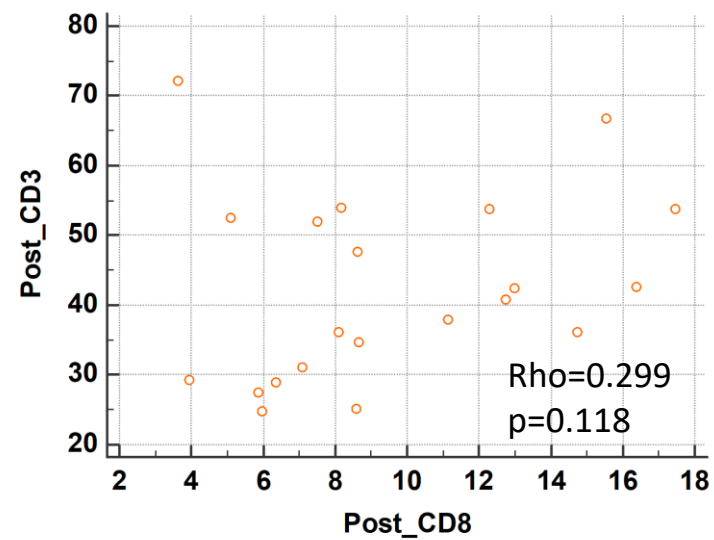
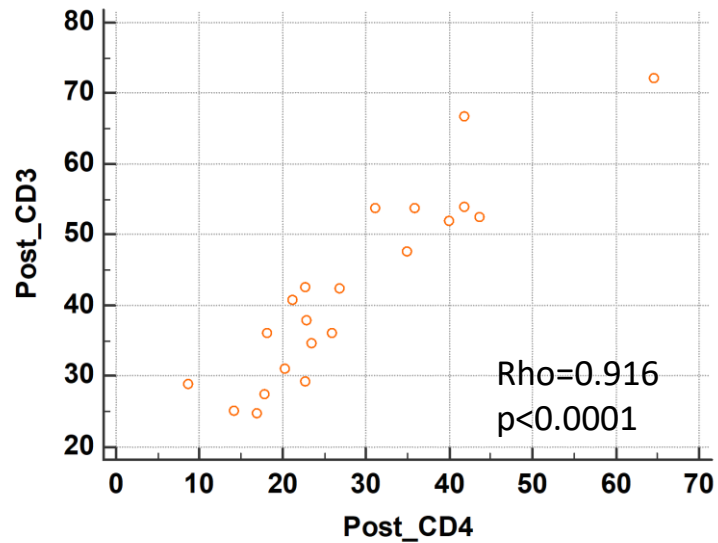
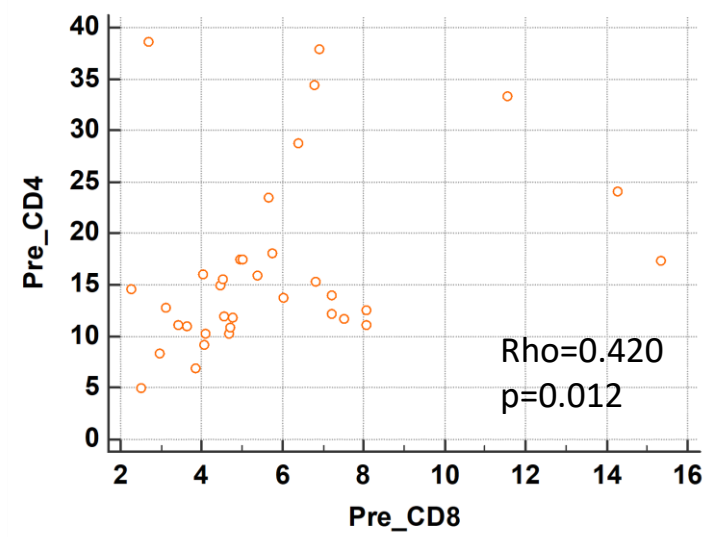
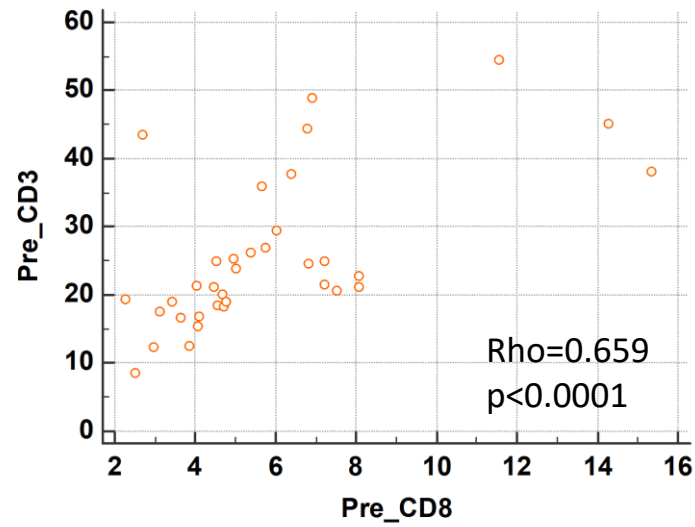
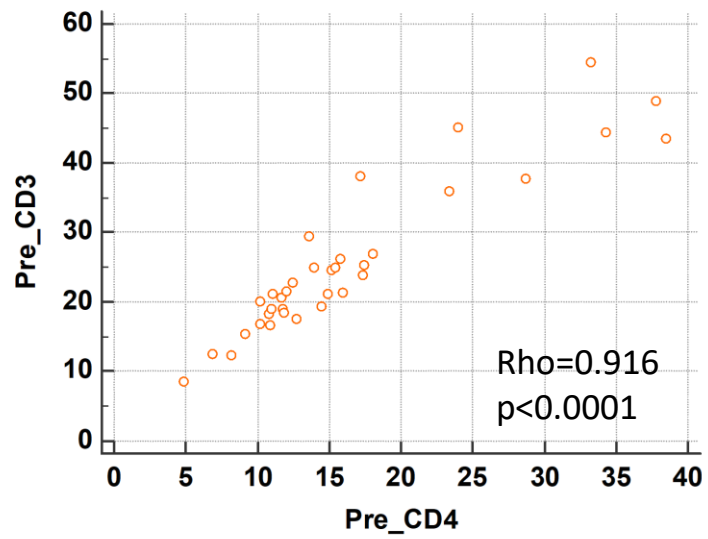
Supplementary Table 1: Characteristics of ICORG 10-05 patients (n=47) included in this study.

	n	%
Total	47	100
Age		
Median (years)	48	
Range (years)	34-80	
Trial Arm		
TCHL	23	48.9
TCH	16	34.1
TCL	8	17.0
ER status		
Negative	17	36.2
Positive	30	63.8
PR status		
Negative	27	57.4
Positive	20	42.6
Treatment outcome		
pCR	22	46.8
No pCR	25	53.2

TC – docetaxel/carboplatin, H – trastuzumab, L – lapatinib, ER- estrogen receptor, PR-progesterone receptor, pCR – pathological complete response.

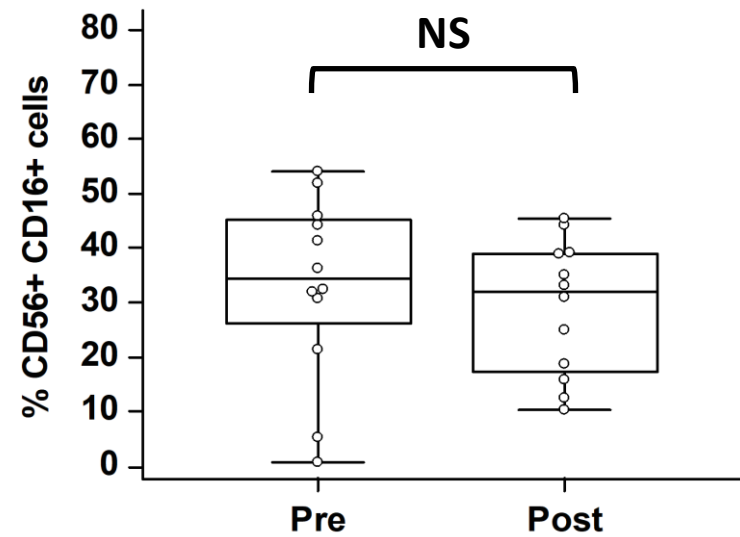


Supplementary Figure 1. Pre-treatment *in vitro* trastuzumab-mediated ADCC levels induced by PBMCs from ICORG 10-05 patients against SKBR3 cells based on SNP status. F= phenylalanine, V = valine, Q = glutamine, H= histadine, R=arginine, D= aspartic acid , N= asparagine. No significant difference in ADCC levels was detected based on SNP status. rs1050501 was not included as only reference alleles were reported. Independent Student's T test. * $p < 0.05$, NS designates tests that were Not Significant without multiple testing.

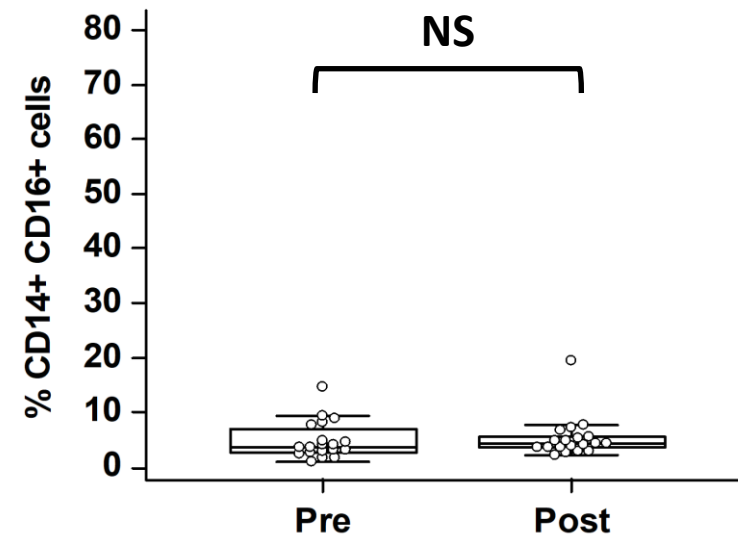


Supplementary Figure 2: Spearman's rho ranked correlation test for CD3+, CD4+ and CD8+ T cell populations in pre-treatment (n=35) and post-treatment (n=21) samples.

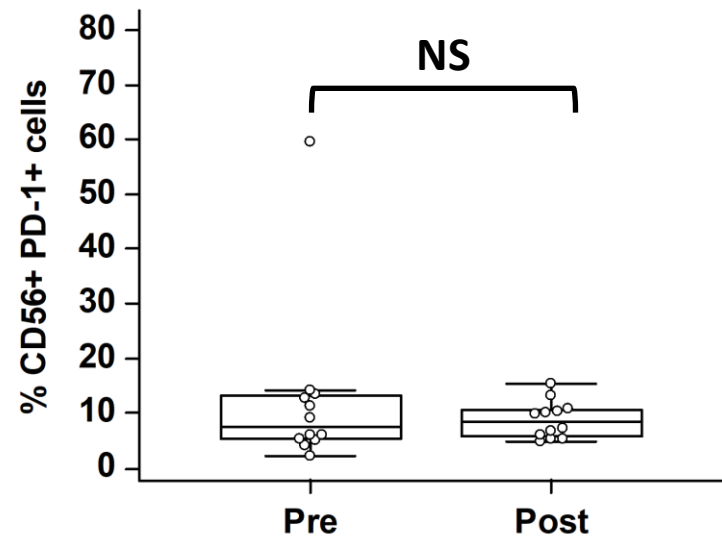
A



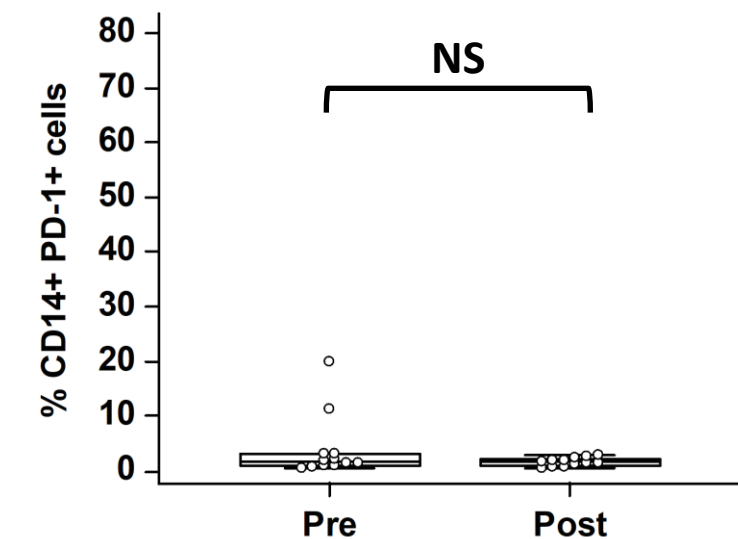
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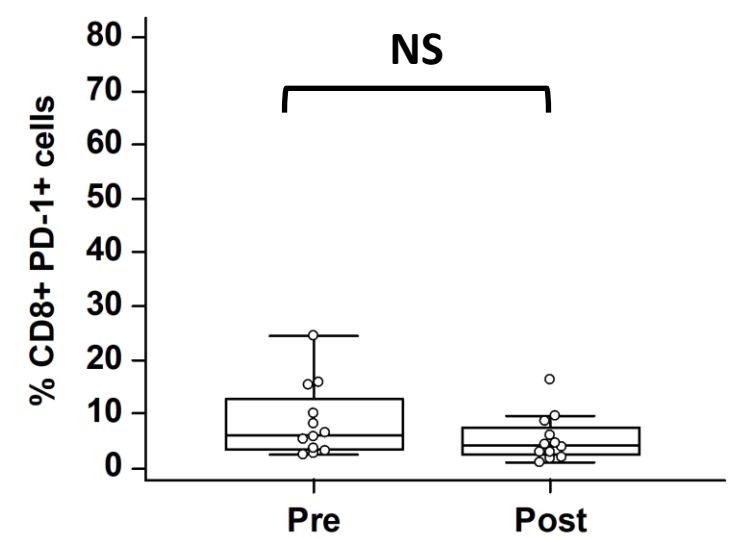
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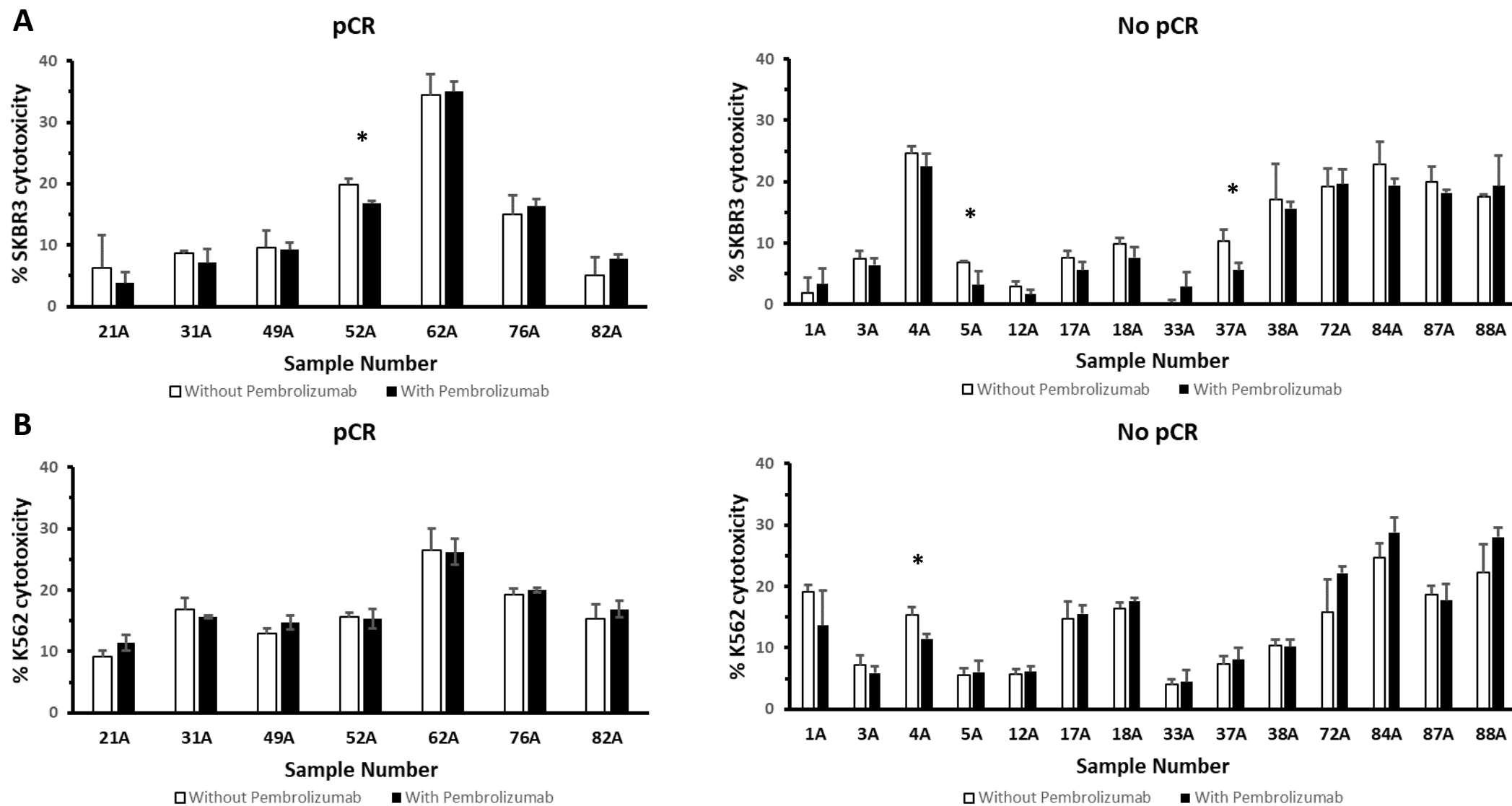
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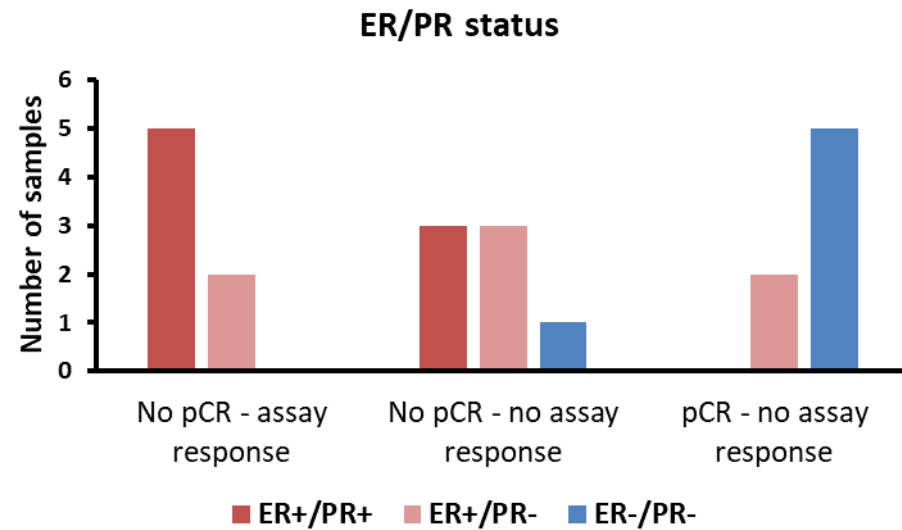
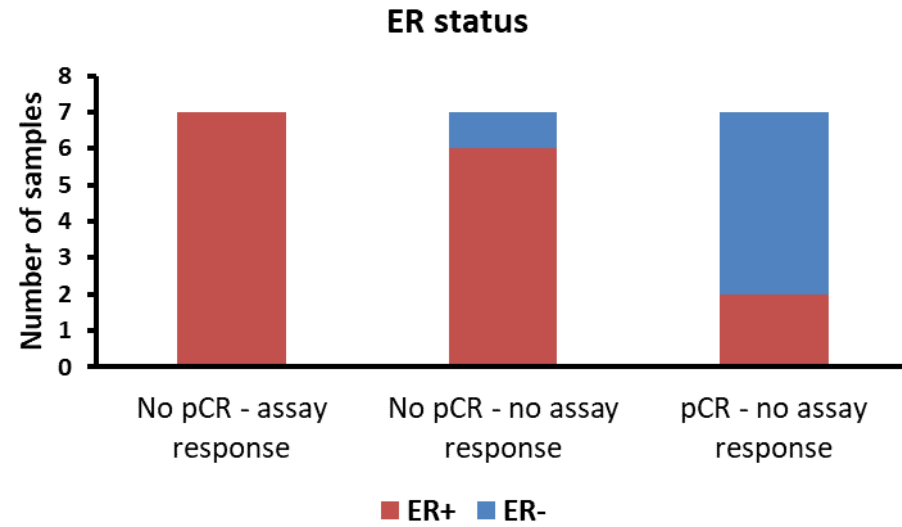
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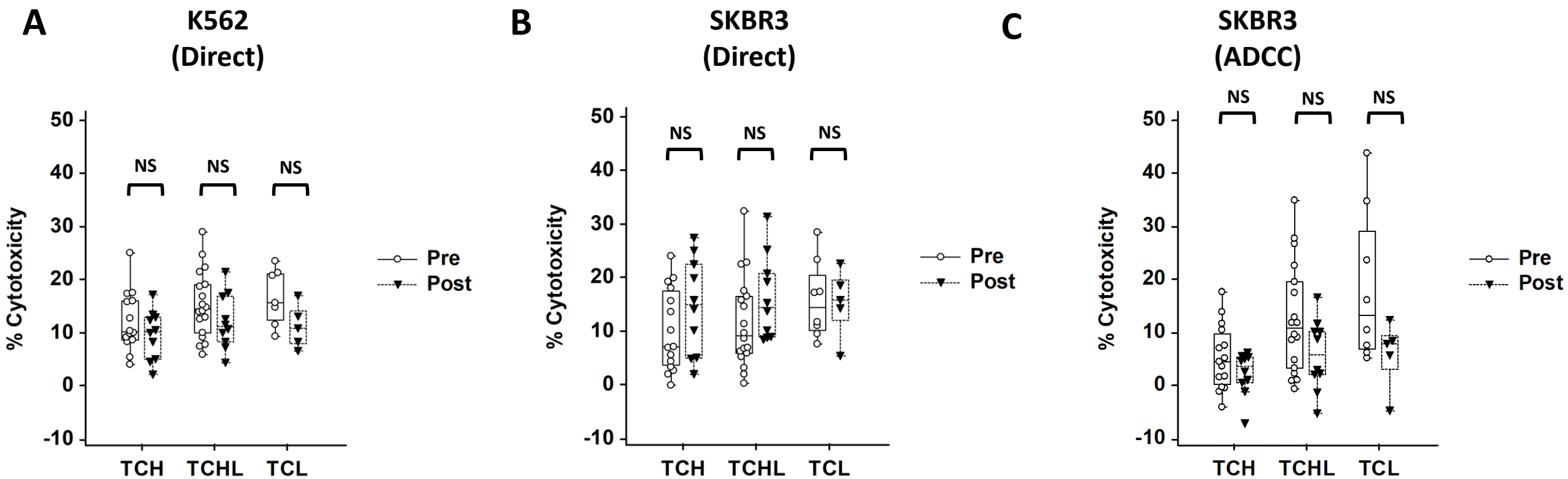
Supplementary Figure 3. Proportion of CD45+ cells staining positive for A) CD56/CD16, B) CD14/CD16, C) CD56/PD-1, D) CD14/PD-1, E) CD8/PD-1 in paired pre-treatment and post-treatment samples. A paired student's t test was used to determine statistical significance, all p values were corrected for multiple testing * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, NS not significant.



Supplementary Figure 4 A) Direct cytotoxicity levels elicited against SKBR3 cells by pre-treatment patient PBMCs from pCR (n=7) and No-pCR (n=14) cohorts with and without pembrolizumab. Effector cells to target cell ratio of 10:1. B) Direct cytotoxicity levels elicited against K562 cells by pre-treatment patient PBMCs from pCR (n=7) and No-pCR (n=14) cohorts with and without pembrolizumab. Effector cells to target cell ratio of 10:1. A paired Student's T test was used to determine statistical significance. * $p < 0.05$



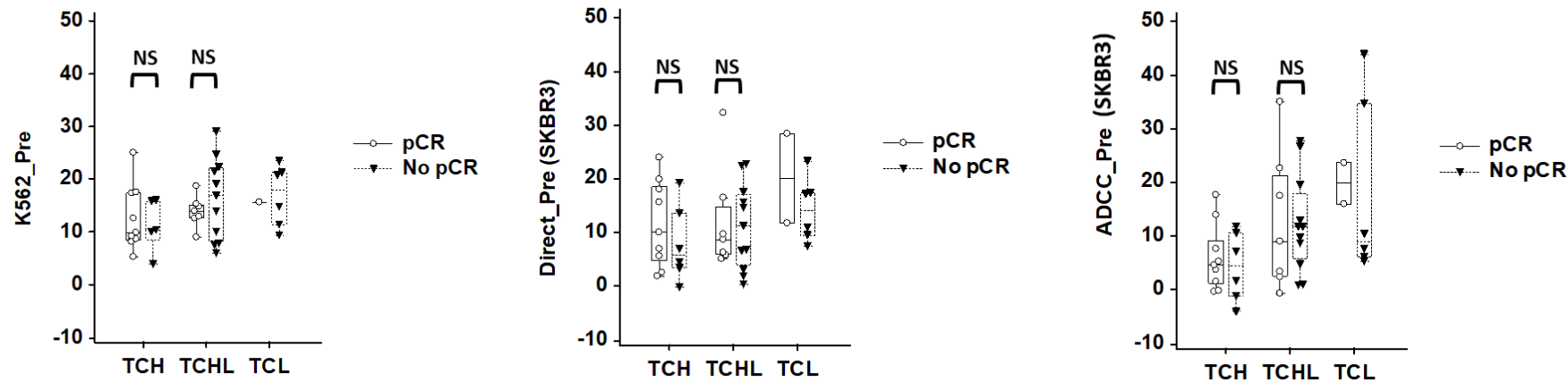
Supplementary Figure 5: Breakdown of ER+ **(A)** and ER+/PR+ **(B)** status of patient samples (n=21) by response in pembrolizumab-ADCC assay/pCR status (Main Figure 6A).



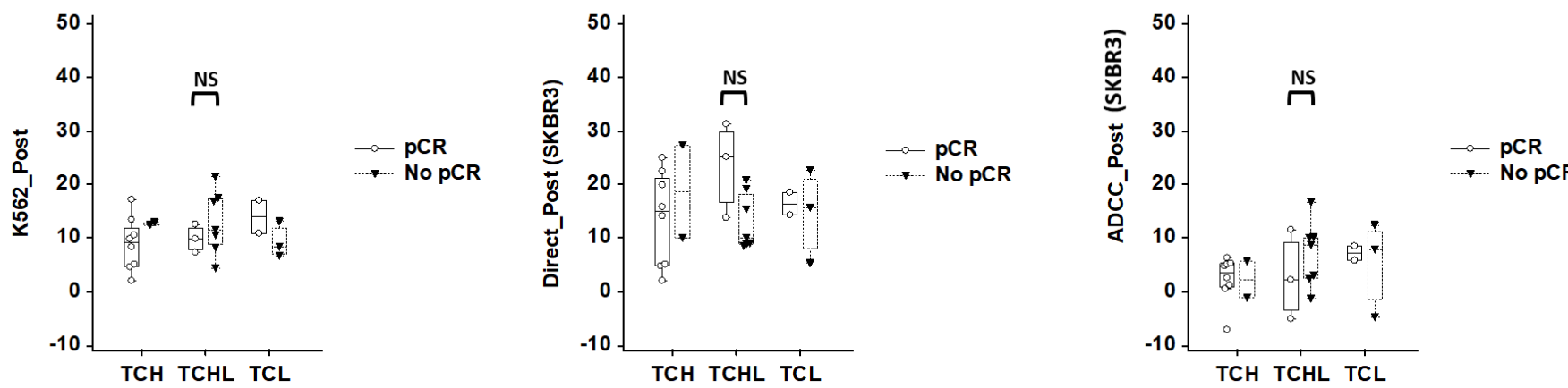
Arm	Assay	Paired Sample (n)	p value	Adjusted p value
TCH	K562	7	0.25	0.55
	Direct (SKBR3)	7	0.03	0.23
	ADCC	7	0.12	0.51
TCHL	K562	7	0.86	0.93
	Direct (SKBR3)	7	0.58	0.87
	ADCC	7	0.20	0.55
TCL	pCR	6	0.72	0.92
	No pCR	15		
	pCR	6	0.37	0.67
	No pCR	15		
PD-1	pCR	4	0.93	0.93
	No pCR	9		

Supplementary Figure 6. Comparison of direct (**A, B**) and antibody-dependent (**C**) cytotoxicity levels of pre- and post-treatment patient PBMCs by treatment arm. TCH, n= 15, TCHL, n= 18, TCL, n= 8. Paired Student's T test. * $p < 0.05$, NS designates tests that were Not Significant.

A

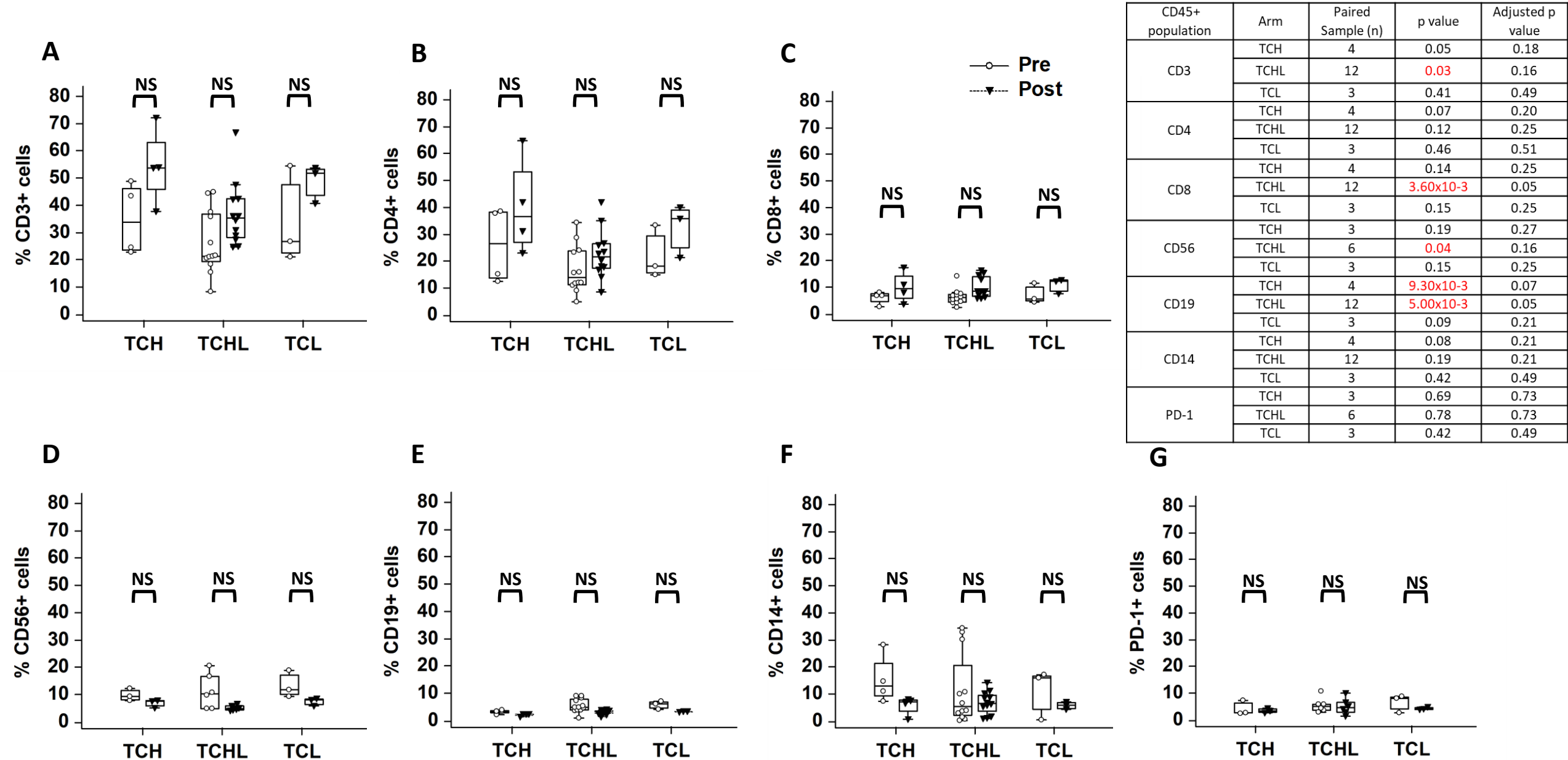


B



Arm	Assay	Pre or Post	pCR (n)	No pCR (n)	p value	Adjusted p value
TCH	K562	Pre	9	5	0.67	0.97
		Post	8	2	0.33	0.96
	Direct (SKBR3)	Pre	9	6	0.38	0.96
		Post	8	2	0.51	0.96
	ADCC	Pre	9	6	0.62	0.97
		Post	8	2	0.97	0.97
TCHL	K562	Pre	7	11	0.47	0.96
		Post	3	7	0.43	0.96
	Direct (SKBR3)	Pre	7	11	0.84	0.97
		Post	3	7	0.05	0.80
	ADCC	Pre	7	11	0.94	0.97
		Post	3	7	0.39	0.96
TCL	K562	Pre	1	6	n/a	n/a
		Post	2	3	0.27	0.96
	Direct (SKBR3)	Pre	2	6	0.37	0.96
		Post	2	3	0.80	0.97
	ADCC	Pre	2	6	0.89	0.97
		Post	2	3	0.79	0.97

Supplementary Figure 7. Comparison of direct (K562 and SKBR3)) and antibody-dependent (SKBR3) cytotoxicity levels for pCR and No pCR patient PBMCs by treatment arm for both pre- **(A)** and post **(B)**-treatment samples. Pre-sample numbers – TCH, n= 15, TCHL, n= 18, TCL, n= 8. Post-sample numbers TCH, n= 10, TCHL, n= 10, TCL, n= 5. An unpaired Student’s T test was used to determine statistical significance for pCR vs No pCR samples in groups with a minimum of n=3. No comparison provided a statistically significant difference ($p < 0.05$), with those groups tested marked as NS (not significant).



Supplementary Figure 8. Percentage of CD45+ cells staining positive for A) CD3, B) CD4, C) CD8, D) CD56+, E) CD19, F) CD14, and G) PD-1+ in paired TCH (n=4), TCHL (n= 12) and TCL (n=3) samples. A paired student's t test was used to determine statistical significance, all p values were corrected for multiple testing, * p < 0.05. † TCH (n=3), TCHL (n=6) and TCHL (n=3)