Supplementary Tables and Figures

Assay	Biomarker	Endpoint	Group*	Effect** (95% CI)	Interaction p (q) value
Luminex	**IL-13**	Week 44 VL	25%-ile	-0.615 (-1.142, -0.088)	**0.003 (0.009)**
			75%-ile	0.222 (-0.318, 0.762)	
	MIP1β	Week 52 CD4 count	25%-ile	0.026 (-0.068, 0.120)	**0.020 (0.061)**
			75%-ile	0.088 (0.002, 0.174)	
	IL-13 binary	Week 48 VL	IL-13 < median	-0.490 (-1.174, 0.194)	**0.044(0.060)**
			IL-13 > median	0.504 (-0.215, 1.222)	
	IFN-γ binary	Week 44 VL	IFN-γ < median	-0.632 (-1.241, -0.022)	**0.019(0.078)**
			IFN-γ >= median	0.424 (-0.272, 1.119)	
	IL-17 binary	Week 44 CD4 count	IL-17 < median	0.100 (0.000, 0.200)	**0.003(0.015)**
			IL-17 >= median	-0.091 (-0.169, -0.014)	
CFSE	**Total**	Week 44 VL	25%-ile	-0.584 (-1.187, 0.020)	**0.004(0.009)**
			75%-ile	0.295 (-0.280, 0.869)	
		Week 48 VL	25%-ile	-0.837 (-1.482, -0.193)	**0.008(0.017)**
			75%-ile	0.015 (-0.577, 0.607)	
	CD4+ binary	Week 52 CD4 count	CD4+ < median	-0.085 (-0.215, 0.045)	**0.018(0.053)**
			CD4+ >= median	0.131 (0.004, 0.259)	

Table S1. Summary of wk28 immunological predictors of preART-unadjusted Vacc-4x effect. *Group: for continuous markers, Group indicates the 25th and 75th percentiles of the identified marker; for binary markers, Group indicates the dichotomized subgroups based on the identified marker. **Effect: the effect was estimated as the $\log_{10}$ difference between Vacc-4x and placebo in the given group.

Assay	Biomarker	Endpoint	Group	Effect* (95% CI)	Interaction p (q) value
Luminex	**TNF-α binary**	Week 48 CD4 count	TNF-α < median	-0.071 (-0.215, 0.074)	**0.009 (0.009)**
			TNF-α >= median	0.192 (0.060, 0.324)	

Table S2. Summary of wk28/wk1 immunological predictors of pre-ART-adjusted Vacc-4x effect.

*Effect: the effect was estimated as the $\log_{10}$ difference between Vacc-4x and placebo in the given Group.

Assay	Biomarker	Endpoint	Group	Effect* (95% CI)	Interaction p (q) value
Luminex	**TNF-α binary**	Week 52 CD4 count	TNF-α < median	-0.039 (-0.176, 0.098)	**0.024 (0.096)**
			TNF-α >= median	0.200 (0.030, 0.371)	
	MIP1β	Week 52 CD4 count	25%-ile	0.038 (-0.085, 0.161)	**0.043 (0.087)**
			75%-ile	0.106 (-0.006, 0.218)	

Table S3. Summary of wk28 immunological predictors of preART-adjusted Vacc-4x effect.

*Effect was estimated as the $\log_{10}$ difference between Vacc-4x and placebo in the given group.

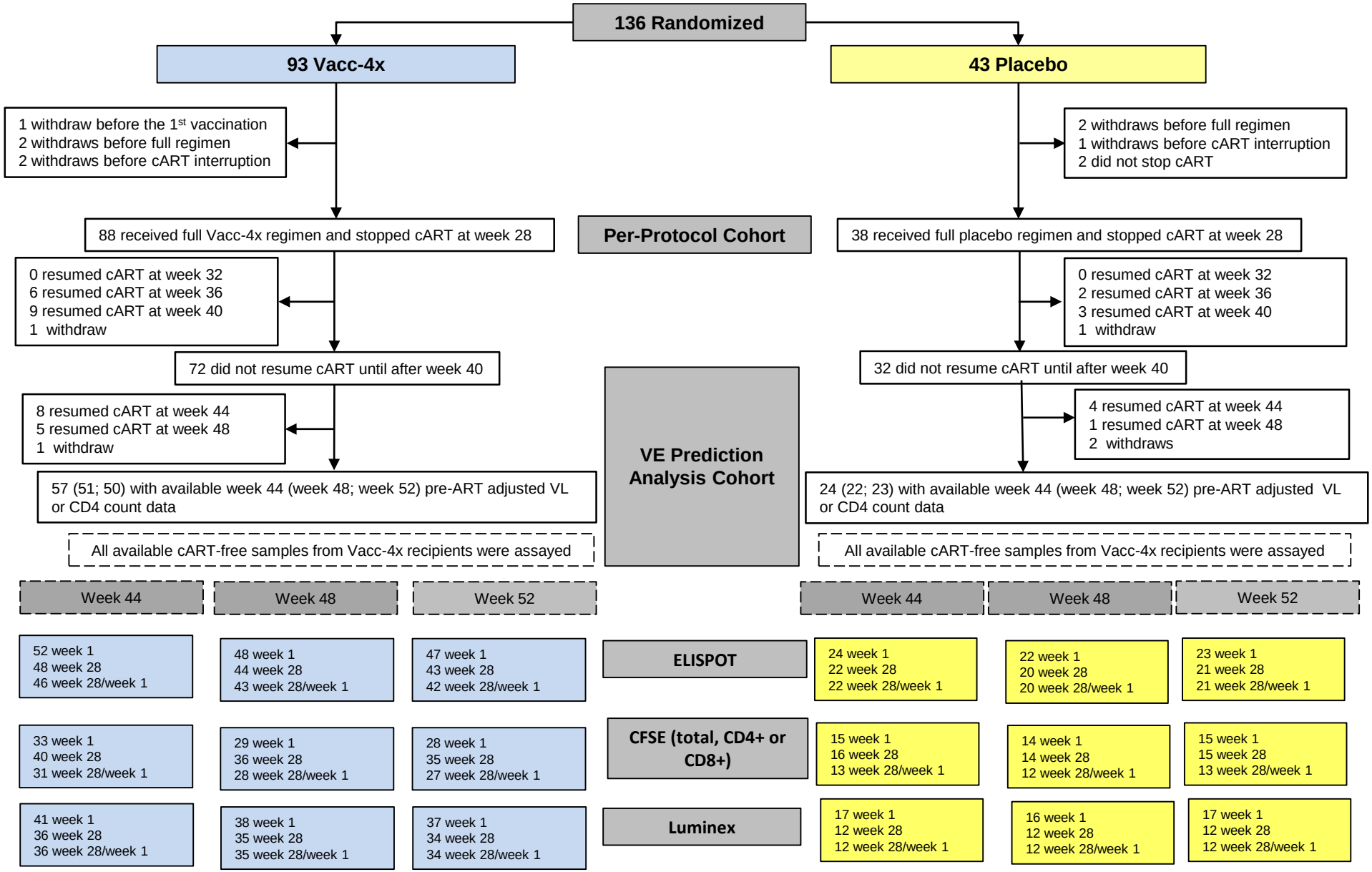

Figure S1. Immunological sample availability for the vaccine effect (VE) prediction analysis of the phase 2 Vacc-4x clinical study for participants with preART values.

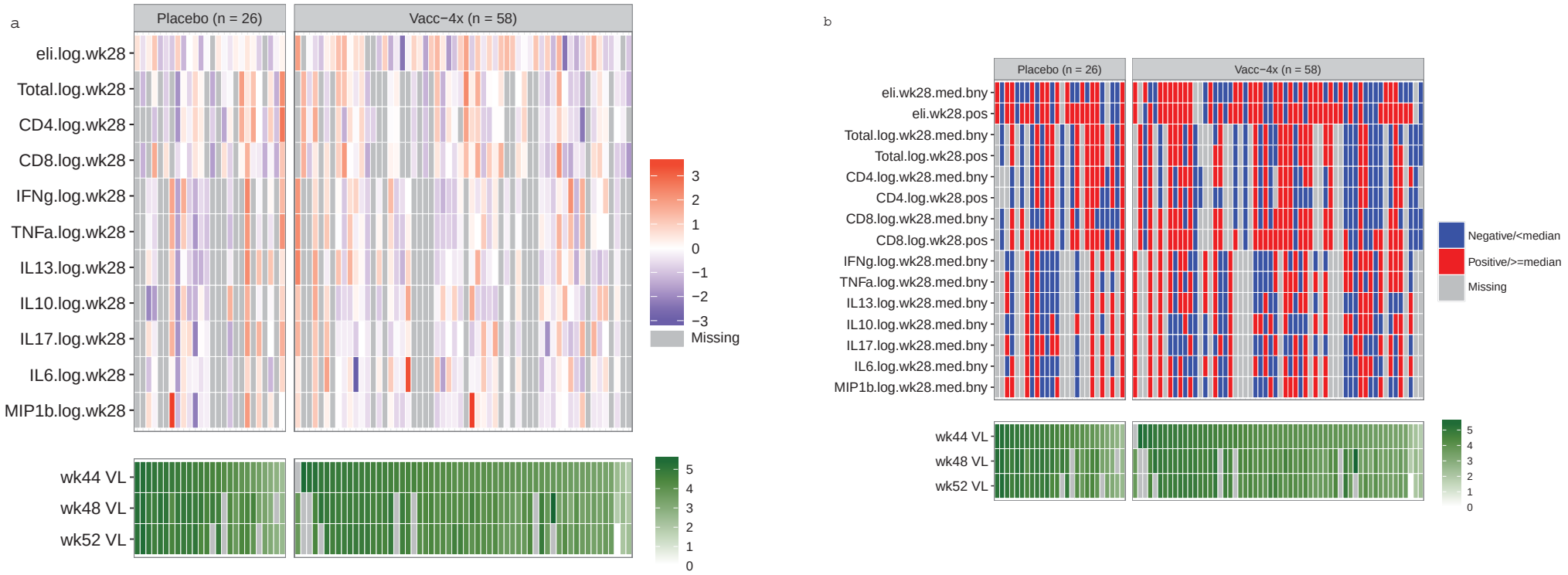

Figure S2. Distributions of immune response variables (wk28) in relation to Weeks 44, 48, and 52 VL values in the placebo and Vacc-4x groups. Each cell indicates the magnitude of each variable (row) for each placebo or Vacc-4x recipient (column) in color grade, where darker red indicates a higher level and darker blue indicates a lower level. Gray shading indicates missing data. The columns are ordered by Week 52 VL, separately within the placebo and Vacc-4x groups. Panel (a) shows mean-centered magnitude of each measurement in standard deviation scale for each continuous marker in relation to VL ($\log_{10}$-scale); Panel (b) shows dichotomized status of each measurement based on median-cutoff (indicated with a suffix “med.bny”) or positivity (indicated with a suffix “pos”) in relation to VL ($\log_{10}$-scale). Patients are ordered such that VL decreases from left to right.

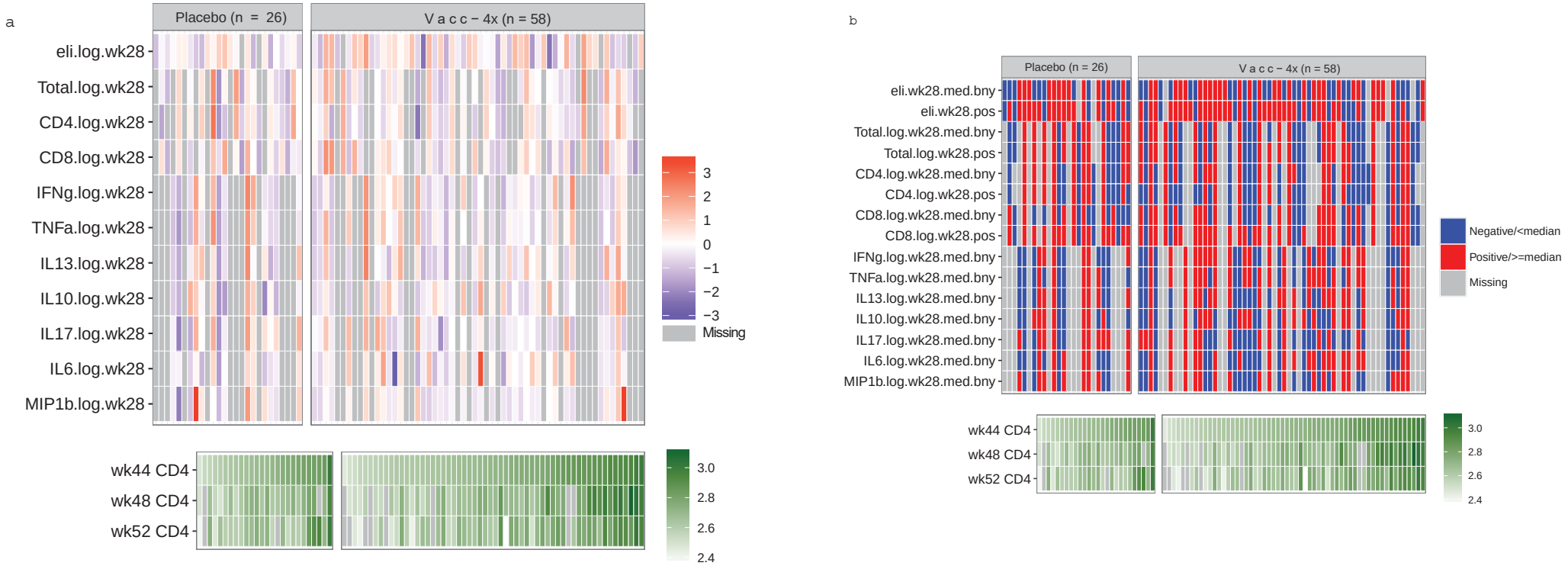

Figure S3. Distributions of immune response variables (wk28) in relation to Weeks 44, 48 and 52 CD4 count values in the placebo and Vacc-4x groups. Each cell indicates the magnitude of each measurement (row) for each placebo or Vacc-4x recipient (column) in color grade, where darker red indicates a higher level and darker blue indicates a lower level. Gray shading indicates missing data. The columns are ordered by Week 52 CD4 count, separately within the placebo and Vacc-4x groups. Panel (a) shows mean-centered magnitude of each measurement in standard deviation scale for each continuous marker in relation to CD4 count ($\log_{10}$-scale); Panel (b) shows dichotomized status of each measurement based on median-cutoff (indicated with a suffix "med.bny") or positivity (indicated with a suffix "pos") in relation to CD4 count ($\log_{10}$-scale).

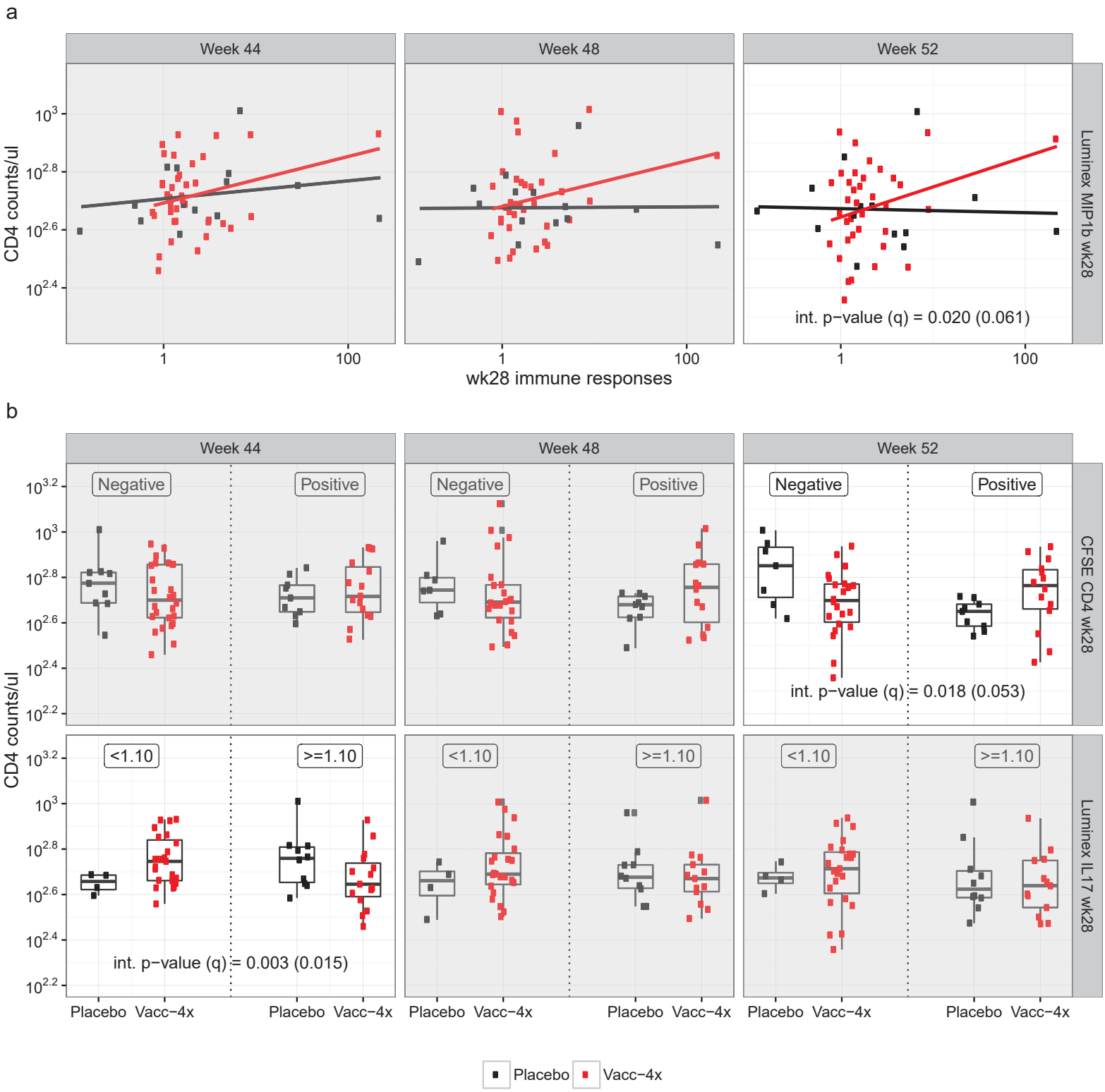

Figure S4. Distributions of CD4 count by identified week28 immunological predictors of vaccine effect. Panel (a) shows CD4 count vs. wk28 Luminex MIP1b; Panel (b) shows the distribution of CD4 count by treatment group for wk28 CFSE CD4 negative and positive responders, and for wk28 Luminex IL17 < and >= median (1.1 $\log_{10}$).

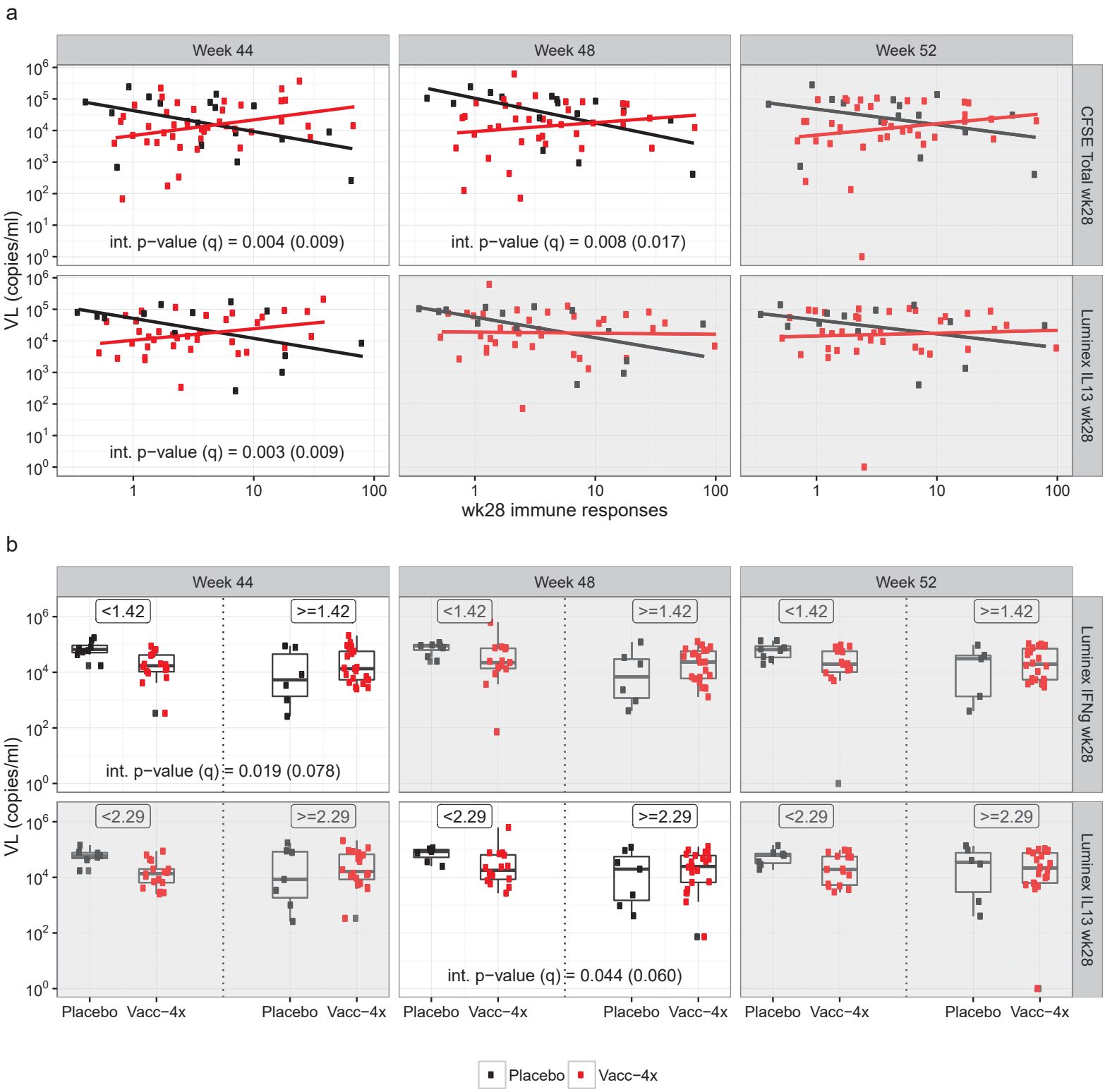

Figure S5. Distributions of VL by identified week28 immunological predictors of vaccine effect. Panel (a) shows VL vs. wk28 CFSE total and Luminex IL-13; Panel (b) shows the distribution of VL by treatment group for wk28 Luminex IFN-γ < and >= median (1.42 $\log_{10}$), and for wk28 Luminex IL13 < and >= median.

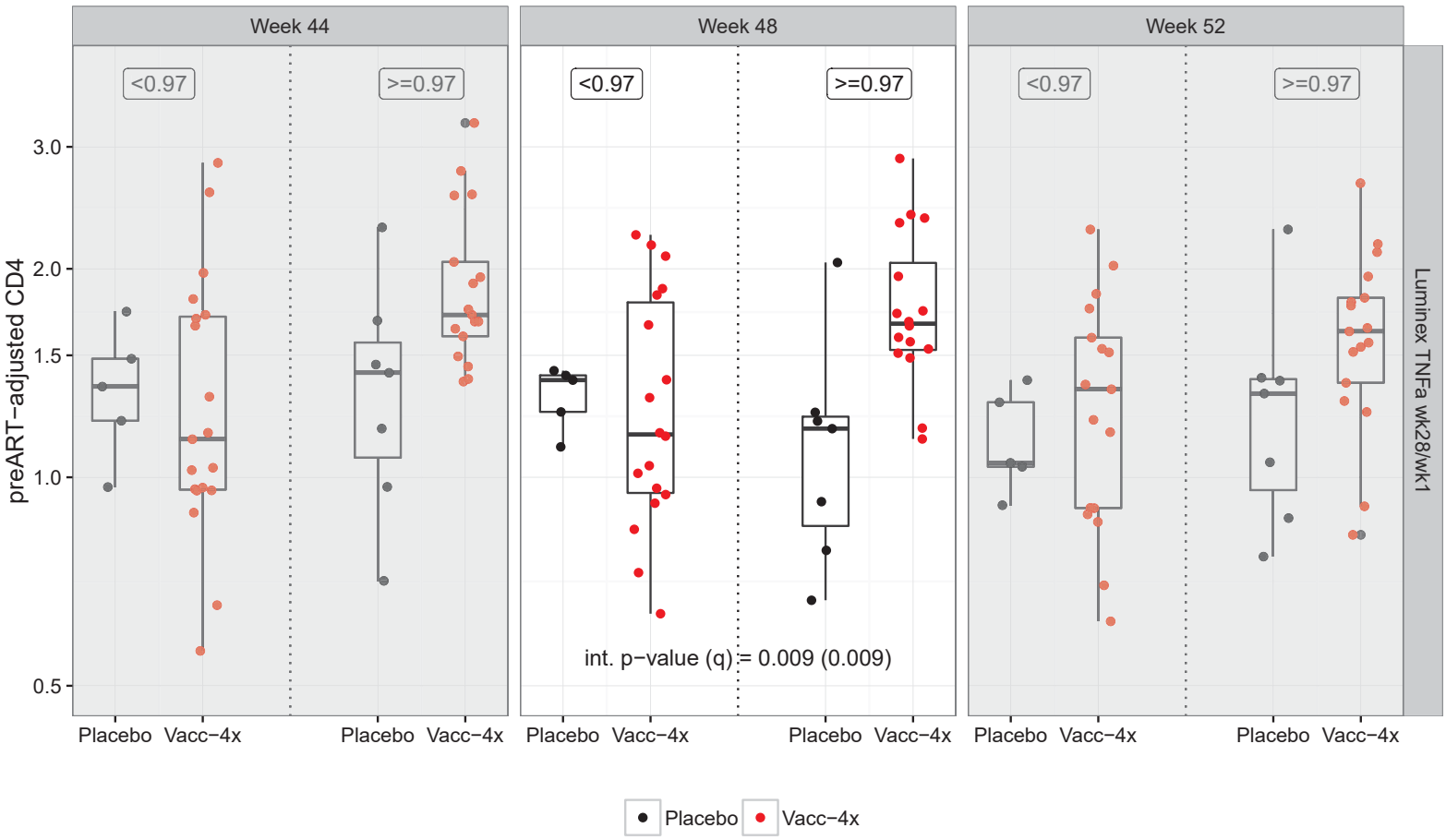

Figure S6. Distributions of preART-adjusted CD4 count by treatment group for wk28/wk1 TNF-α < and >= median (0.97 log10).

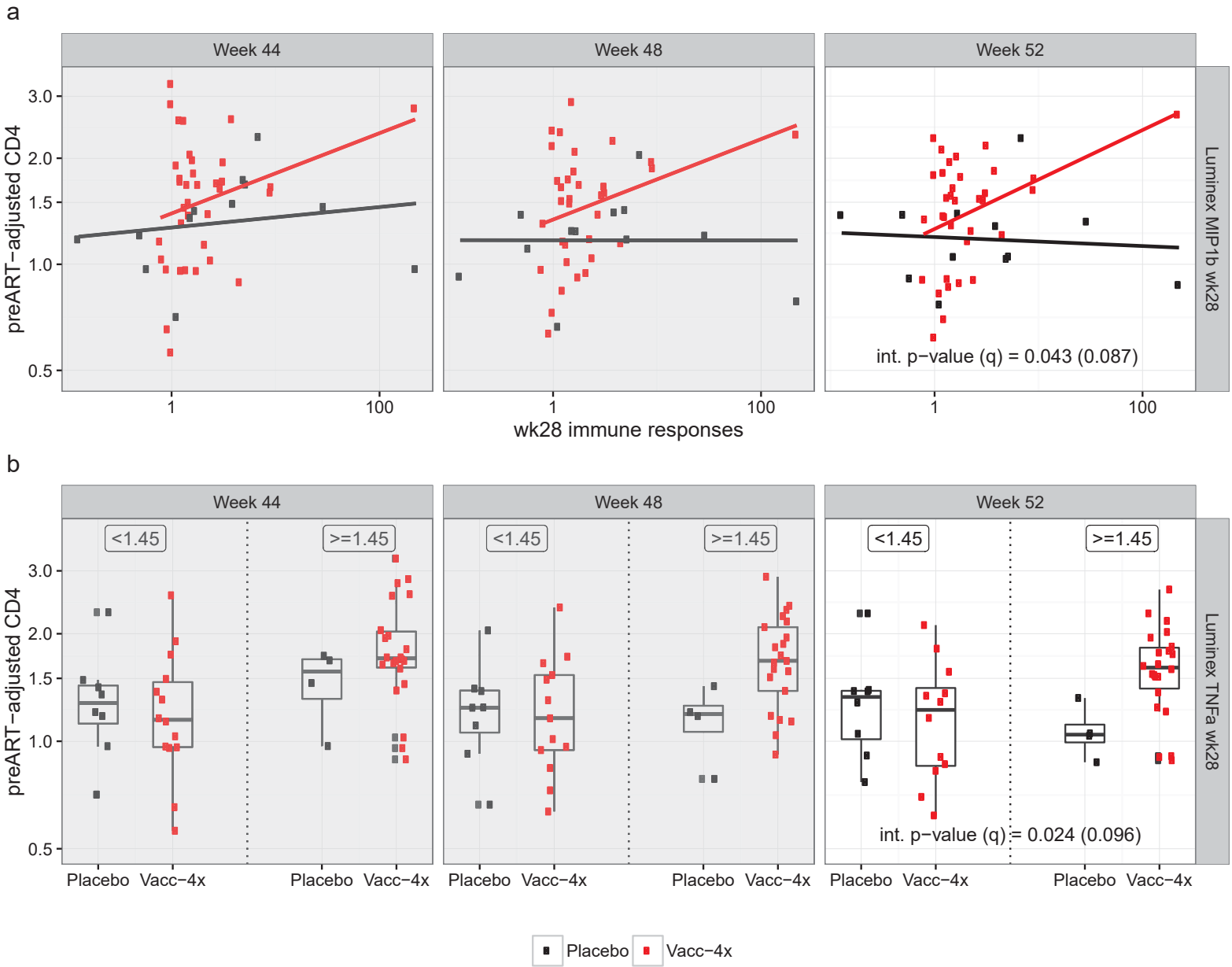

Figure S7. Distributions of preART-adjusted CD4 count by identified week28 immunological predictors of vaccine effect.

Panel (a) shows preART-adjusted CD4 count vs. wk28 Luminex MIP1β; Panel (b) shows the distribution of preART-adjusted CD4 count by treatment group for wk28 Luminex TNF-α < and >= median (1.45 $\log_{10}$).