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Supplemental information

Neutralization breadth of SARS-CoV-2 viral variants following primary series and booster SARS-CoV-2 vaccines in patients with cancer

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Supplemental Information

Figure S1: Concentration of antibodies against SARS-CoV-2 spike protein receptor binding domain (RBD) of a) IgA/M/G total, b) IgA, c) IgG and d) IgM isotypes. Related to Figure 1.

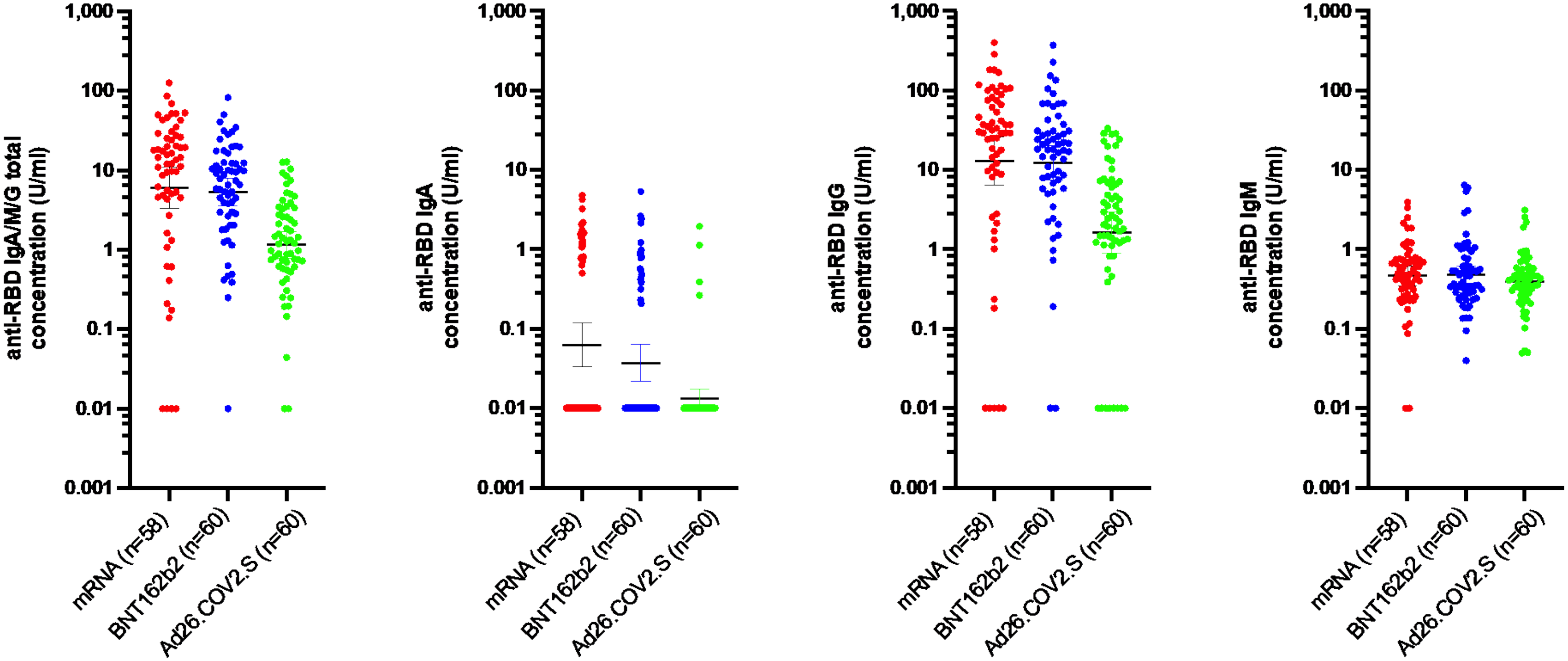

Figure S2: Correlation between neutralization of wildtype SARS-CoV-2 pseudovirus and A) anti-spike or B) anti-RBD antibody concentration. Related to Figure 1.

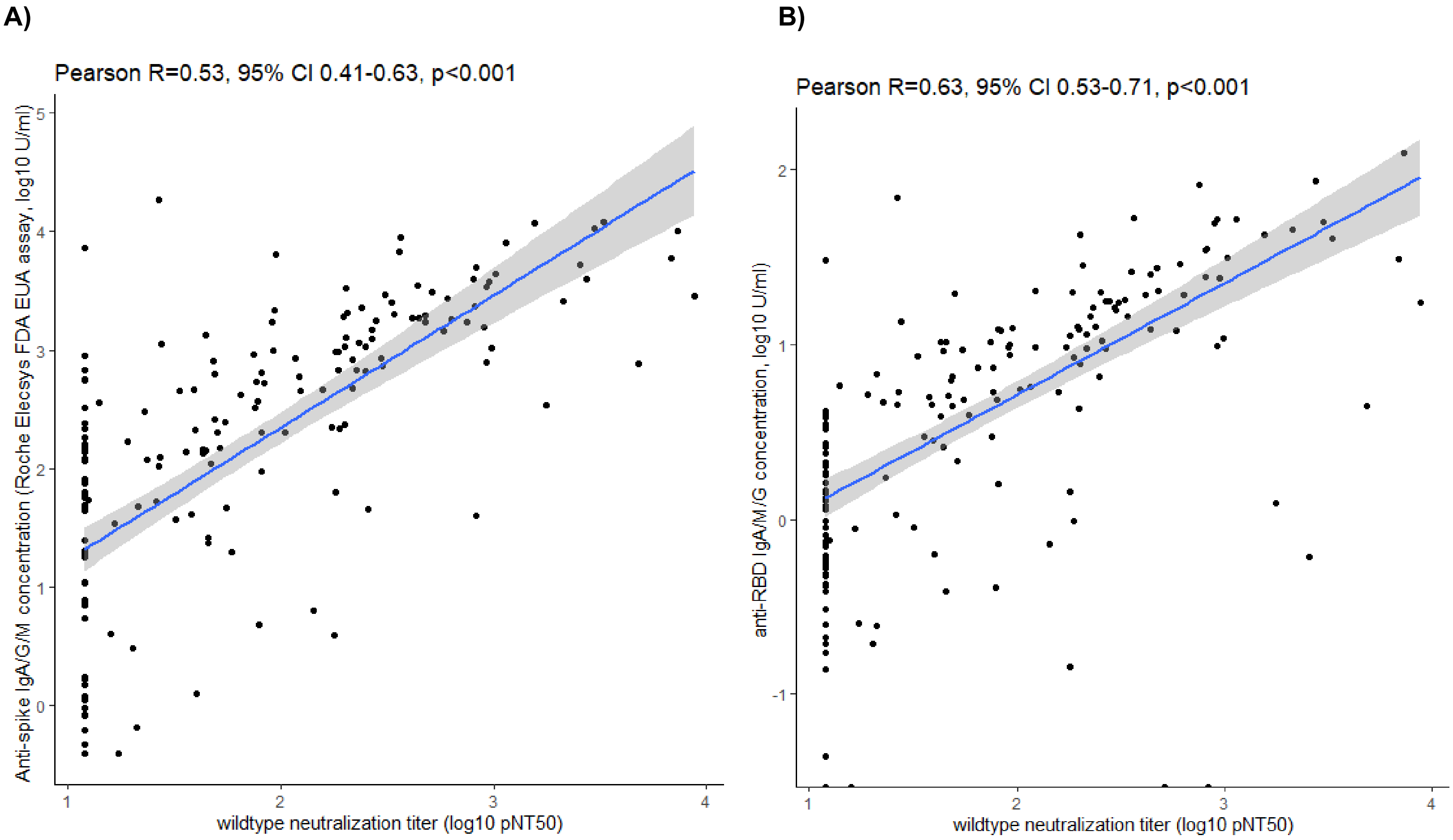

Figure S3: Association between anti-spike IgA/G/M concentration (Roche Elecsys assay) and neutralization breadth. Related to Table 2. Variant neutralization was defined as neutralization >20 for each variant. A horizontal line is drawn at an antibody concentration of $3\log_{10}$ (1000 U/mL), which corresponds to a positive predictive value(PPV) of 90% for >2 variants neutralized.

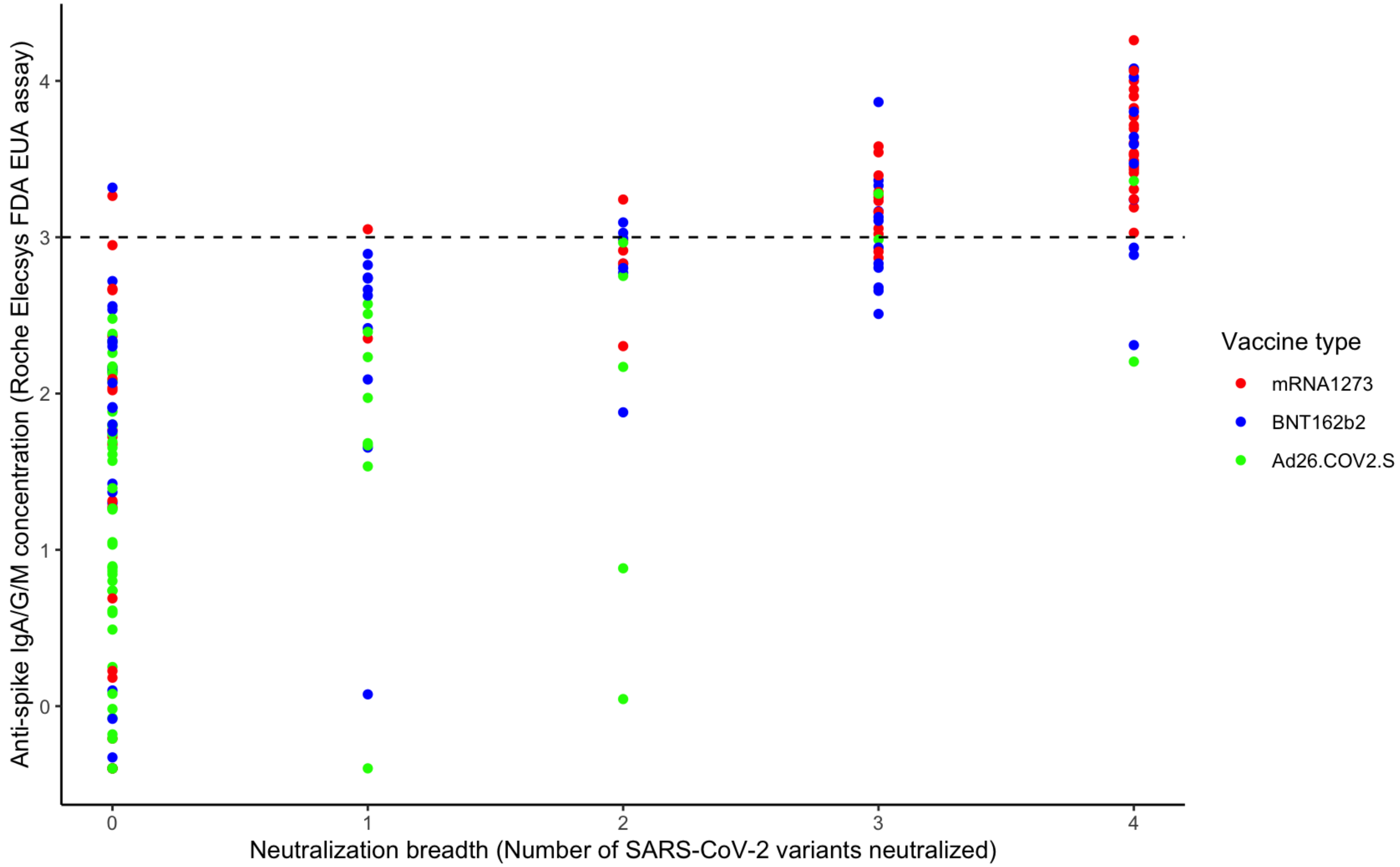

Table S1: Summary of mutations in SARS CoV-2 strains used in this study. Related to STAR Methods, Figure 1 and Figure 2.

Strain/Mutation	L18F	T19R	T20N	P26S	delH69-V70	D80A	D138Y	G142D	delY145	delE156-	R190S	D215G	delL242-L244	K417N	K417T	L452R	T478K	E484K	E484Q	N501Y	A570D	D614G	H655Y	P681H	P681R	A701V	T716I	D950N	S982A	T1027I	D1118H	V1176F	delF1256-T1273
Wildtype																																	+
Alpha B.1.1.7					+				+											+	+	+		+			+		+		+		+
Beta B.1.351 v1						+						+	+	+				+		+		+				+							+
Gamma P.1	+		+	+			+				+				+			+		+		+	+							+		+	+
Delta B.1.617.2 v1		+						+		+						+	+					+			+			+					+

Table S2: Correlates of neutralization of viral variants in patients with cancer. Shown are results of multivariate regression model including the covariates shown, with log10 pseudovirus neutralization of each viral variant as the response variable. Related to Figure 1**.**

	Wildtype			Alpha			Beta			Gamma			Delta		
Characteristic	**Beta**	**95% CI**	**p-value**	**Beta**	**95% CI**	**p-value**	**Beta**	**95% CI**	**p-value**	**Beta**	**95% CI**	**p-value**	**Beta**	**95% CI**	**p-value**
Age	-0.07	-0.12, -0.03	0.002	-0.09	-0.13, -0.04	<0.001	-0.02	-0.05, 0.00	0.061	-0.07	-0.11, -0.02	0.003	-0.04	-0.09, 0.00	0.059
Vaccine type															
mRNA1273	Ref			Ref			Ref			Ref			Ref		
BNT162b2	-0.38	-0.62, -0.15	0.002	-0.33	-0.55, -0.10	0.005	-0.08	-0.21, 0.04	0.2	-0.39	-0.61, -0.16	<0.001	-0.34	-0.57, -0.11	0.003
Ad26.COV2.S	-0.89	-1.1, -0.65	<0.001	-0.6	-0.84, -0.37	<0.001	-0.16	-0.29, -0.03	0.013	-0.6	-0.84, -0.37	<0.001	-0.64	-0.87, -0.40	<0.001
Chemotherapy	-0.28	-0.49, -0.07	0.008	-0.31	-0.51, -0.11	0.002	-0.11	-0.22, -0.01	0.04	-0.26	-0.45, -0.06	0.012	-0.12	-0.32, 0.07	0.2
Immunotherapy	0.08	-0.20, 0.35	0.6	0.02	-0.24, 0.28	0.9	0.06	-0.08, 0.20	0.4	0.04	-0.21, 0.30	0.7	0.04	-0.22, 0.30	0.8
Time after 1st dose (days)	0	-0.03, 0.02	0.7	0.01	-0.01, 0.04	0.2	0.01	0.00, 0.02	0.081	0.01	-0.02, 0.03	0.5	0	-0.03, 0.02	0.8
Cancer type															
Solid	Ref			Ref			Ref			Ref			Ref		
BMT	0.02	-0.28, 0.32	>0.9	0.22	-0.06, 0.51	0.13	0.17	0.02, 0.33	0.031	0.18	-0.11, 0.46	0.2	0.16	-0.13, 0.45	0.3
Heme	-0.15	-0.51, 0.21	0.4	-0.01	-0.36, 0.33	>0.9	-0.02	-0.21, 0.17	0.8	0.03	-0.32, 0.38	0.9	-0.11	-0.45, 0.24	0.5

Table S3: Characteristics of patients who received booster vaccine doses. Related to Figure 2.

	Cancer type, therapy	Initial Vaccine series	Additional vaccine dose type	Interval between initial and additional dose (days)
1	Cutaneous Squamous Cell Carcinoma on immunotherapy	Ad26.COV2.S	BTN162b2	50
2	Breast cancer previously on chemotherapy	Ad26.COV2.S	BTN162b2	81
3	Breast cancer and marginal zone lymphoma on lenalidomide (no B-cell depleting agent)	Ad26.COV2.S	BTN162b2	81
4	Oral squamous cell cancer receiving targeted therapy and steroids	Ad26.COV2.S	BTN162b2	104
5	Lung cancer on immunotherapy and steroids	Ad26.COV2.S	mRNA1273	86
6	Breast cancer on active chemotherapy	mRNA1273	BTN162b2	96
7	Bone marrow transplanted on immunosuppression	mRNA1273	mRNA1273	79
8	Lung cancer, on chemotherapy and steroids	mRNA1273	mRNA1273	115
9	oral squamous cell cancer receiving chemotherapy, immunotherapy and steroids	BTN162b2	BTN162b2	73
10	lung cancer (early stage) receiving chemoradiation	BTN162b2	BTN162b2	80
11	Breast cancer on targeted therapy	BTN162b2	BTN162b2	108
12	Oral squamous cell cancer receiving chemoradiation	BTN162b2	mRNA1273	78
13	Pancreatic cancer receiving chemotherapy	BTN162b2	mRNA1273	88

Code

```
#Analysis of variant neutralization for Naranbhai et al., Cancer Cell 2021

#compute and analyze neutralization breadth and number of measurable isotype antibodies against RBD

breadththreshold=20 #pNT50 threshold of 20 from Garcia-Beltran Cell 2021

var$breadth=ifelse(var$Alpha>breadththreshold,1,0)+ifelse(var$Beta.v1>breadththreshold,1,0)+ifelse(var$Gamma>breadththreshold,1,0)+ifelse(var$Delta>breadththreshold,1,0)


isothreshold=0

var$isotypeswitch=ifelse(var$RBD.IgA>isothreshold,1,0)+ifelse(var$RBD.IgM>isothreshold,1,0)+ifelse(var$RBD.IgG>isothreshold,1,0)

table(var$isotypeswitch, var$covid_vaccine_brand.factor)


#Table 2

tbl_regression(lm(breadth~log10(pNT50_WT)+I(Age/5)+covid_vaccine_brand.factor+Chemotherapy+Immunotherapy+I(SampleDayspost1stdose/7)+strata(cancergroup), var[which(!var$Group=="Post boost"),])) %>%

  add_n()


#Fig S3 how well does spike binding titer predict breadth

cols <- c("Moderna" = "red", "Pfizer" = "blue", "Johnson & Johnson/ Janssen" = "green")

ggplot(var[which(!var$Group=="Post boost"),], aes(x=breadth, y=log10(Spike.resultnum)))+geom_point(aes(color=covid_vaccine_brand.factor))+theme_classic()+ylab("Anti-spike IgA/G/M concentration (Roche Elecsys FDA EUA assay)")+xlab("Neutralization breadth (Number of SARS-CoV-2 variants neutralized)")+guides(color=guide_legend(title="Vaccine type"))+geom_hline(yintercept=3, lty=2)+ scale_colour_manual(values = cols,labels = c("mRNA1273", "BNT162b2", "Ad26.COV2.S"))

#Calculate PPV

library("epiR")

epi.tests(table(var$Spike.resultnum[which(!var$Group=="Post boost")]>1000,var$breadth[which(!var$Group=="Post boost")]>2))
```