

COVID-19: Vaccines and Variants

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Slide Credits

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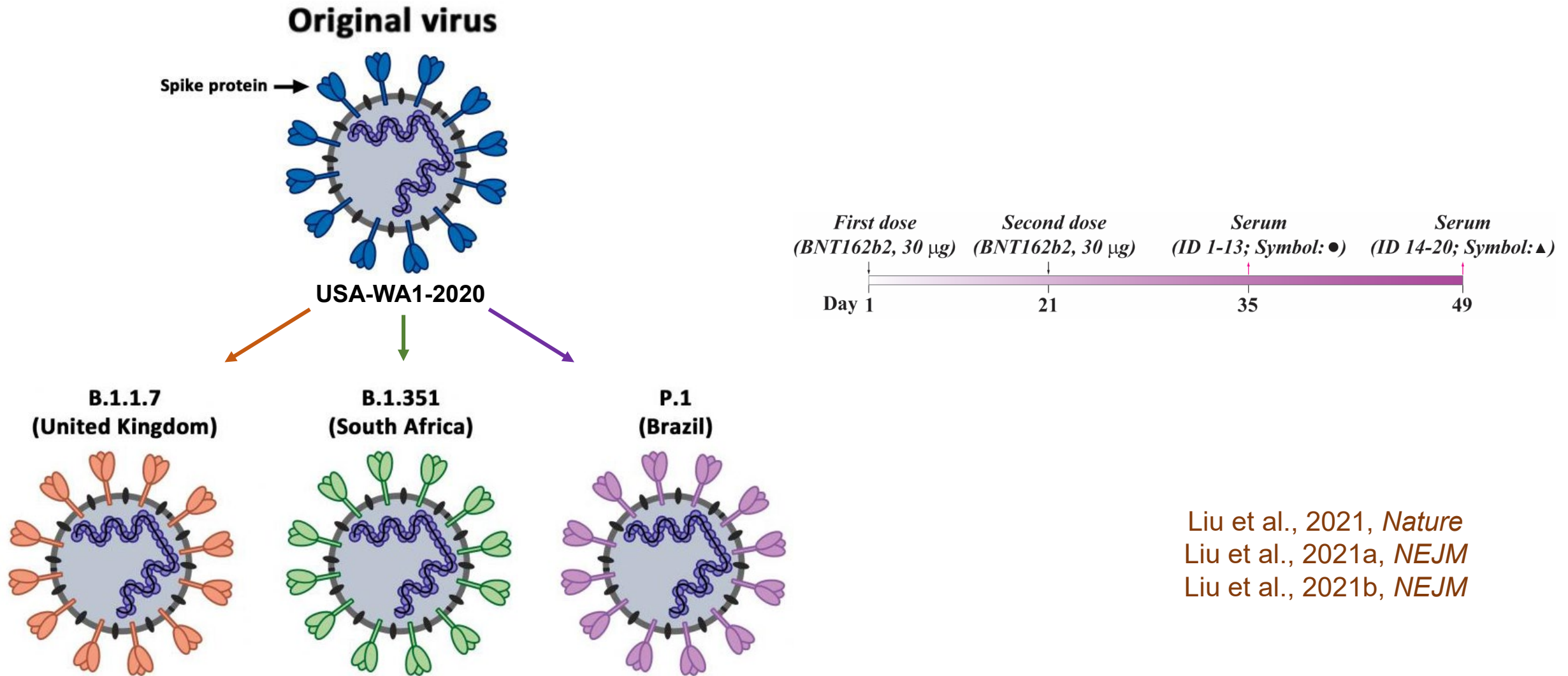
Ragon Institute

MassCPR

NIAID

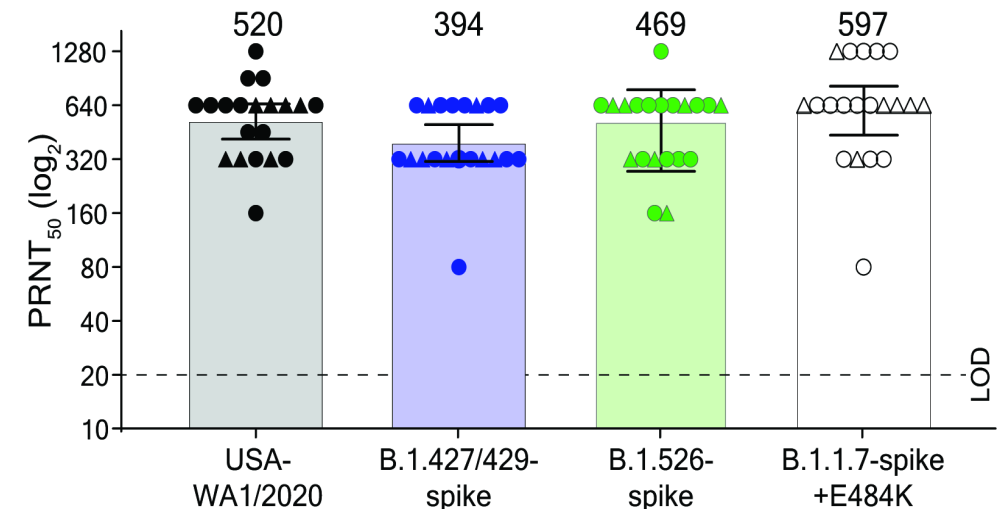
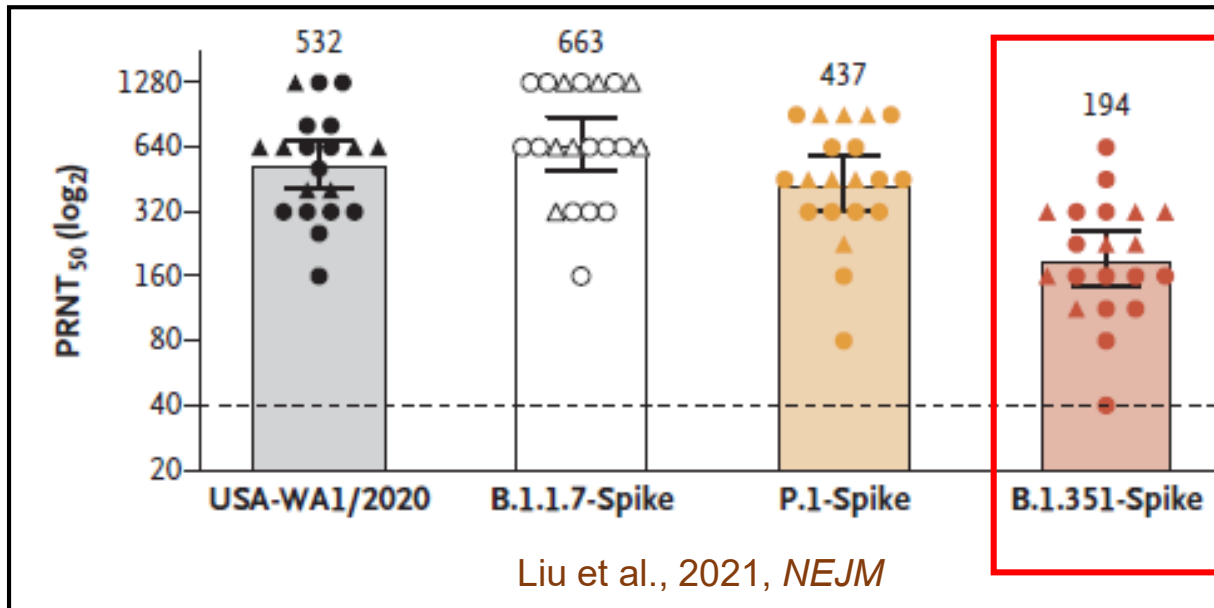
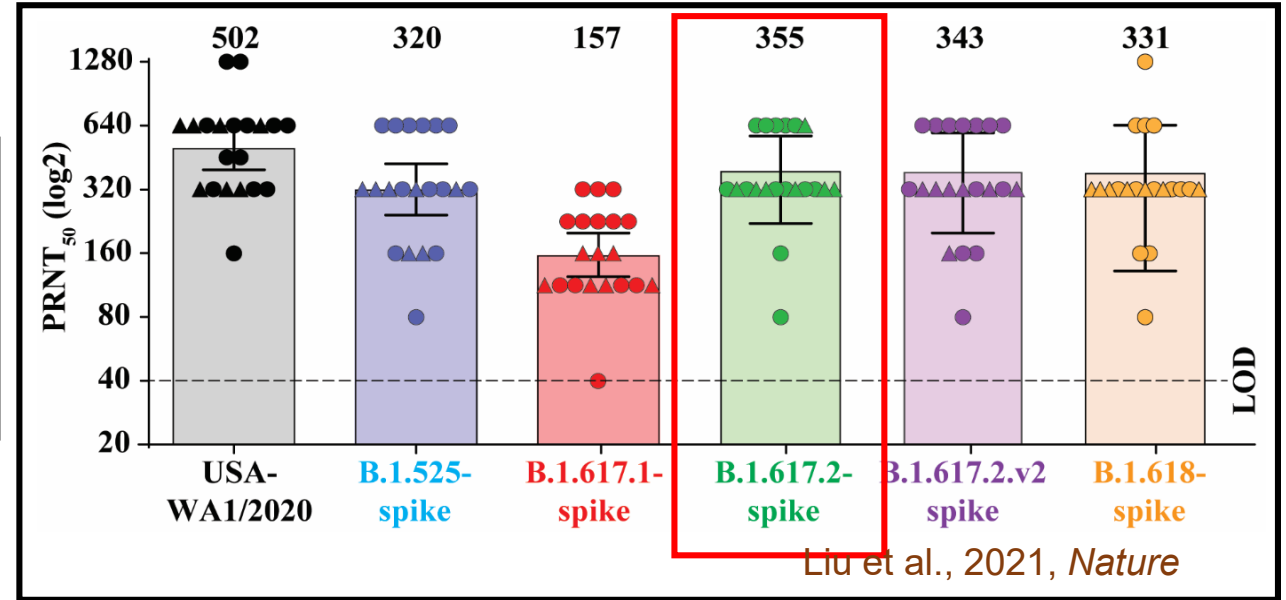
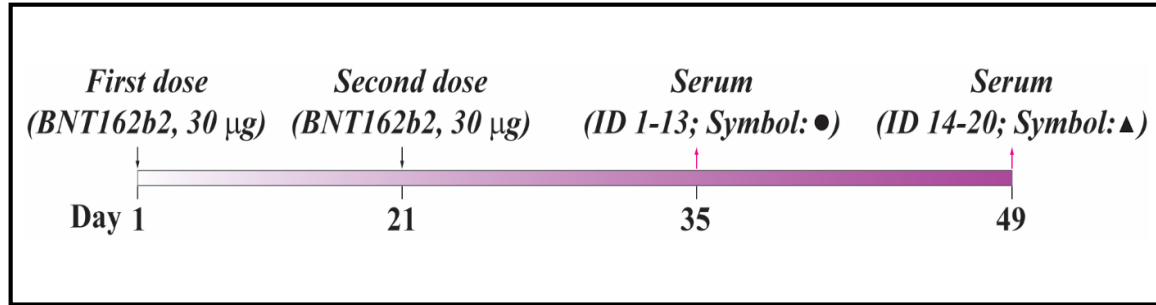
All Trial Volunteers!

Pfizer-BioNTech BNT162b2 Neutralization of SARS-CoV-2 Variants



Liu et al., 2021, *Nature*
Liu et al., 2021a, *NEJM*
Liu et al., 2021b, *NEJM*

Pfizer-BioNTech BNT162b2 Neutralization of SARS-CoV-2 Variants

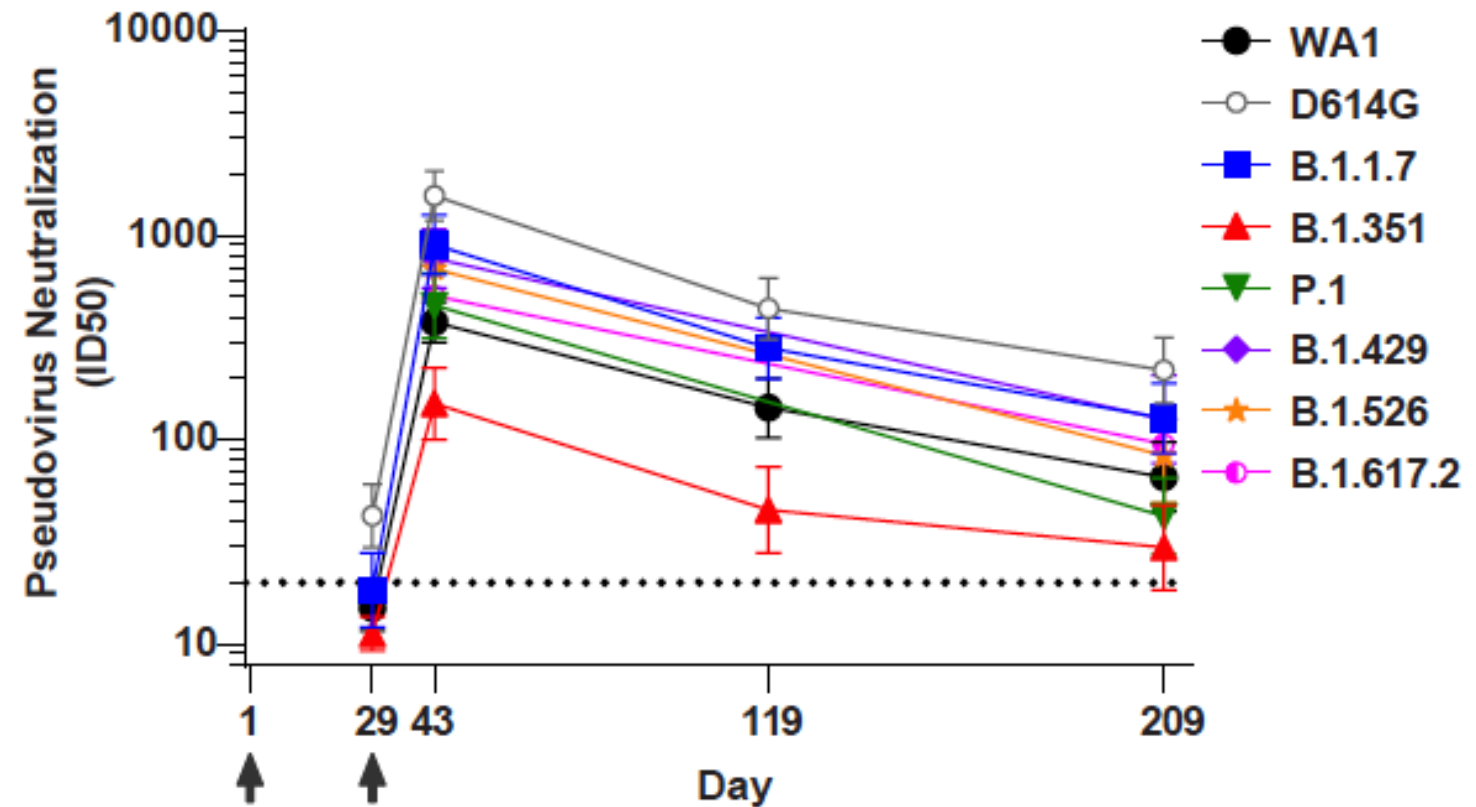


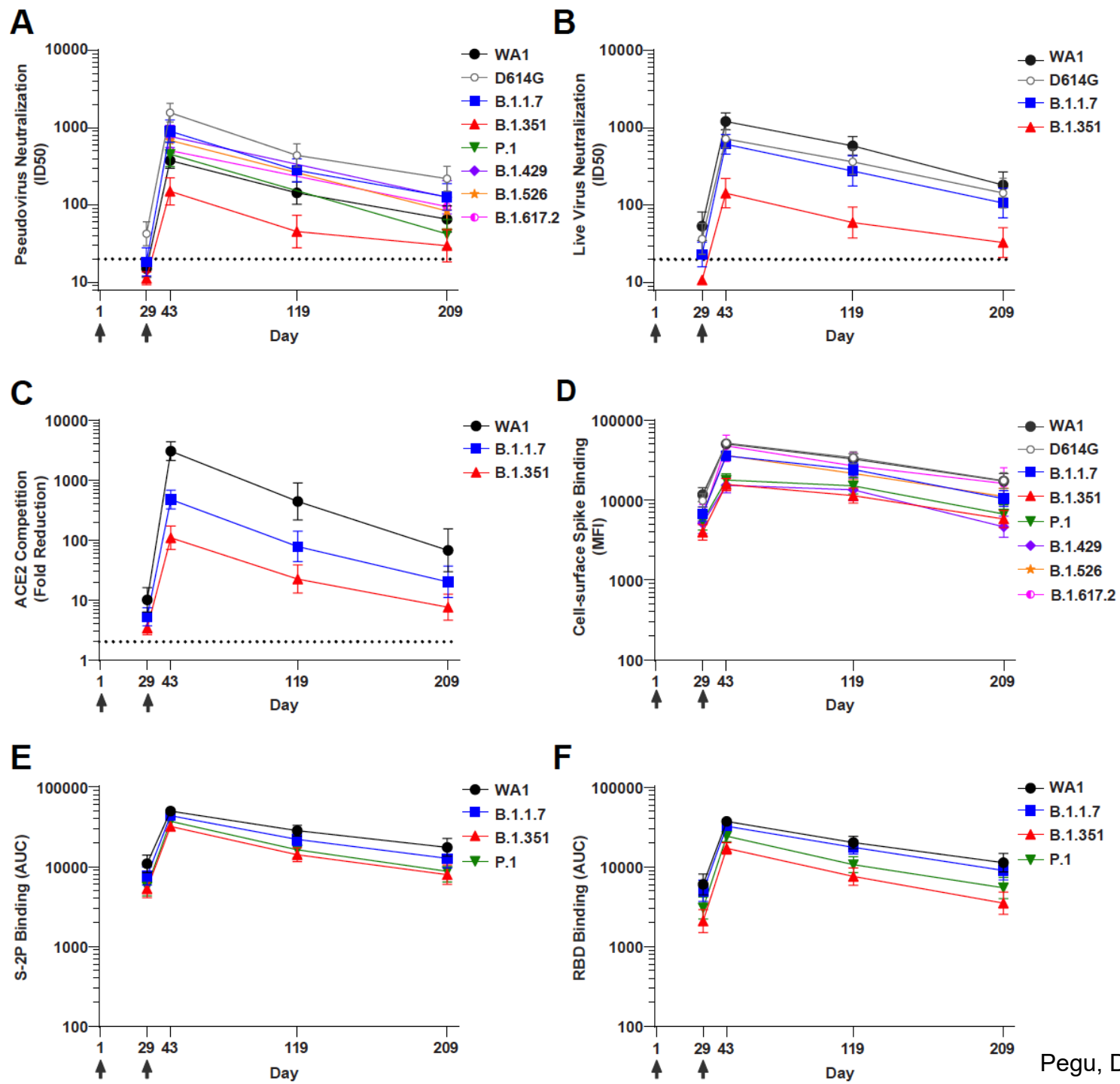
Pfizer-BioNTech BNT162b2: Coverage of Variants

- Cross-reactive neutralizing responses robust at peak immunity after the second dose
- Responses observed to all variants, but 2-4 fold decline to B.1.351 and approximately 2 fold decline to B.1.617.2
- Durability data pending

Moderna mRNA-1273 Neutralization of SARS-CoV-2 Variants

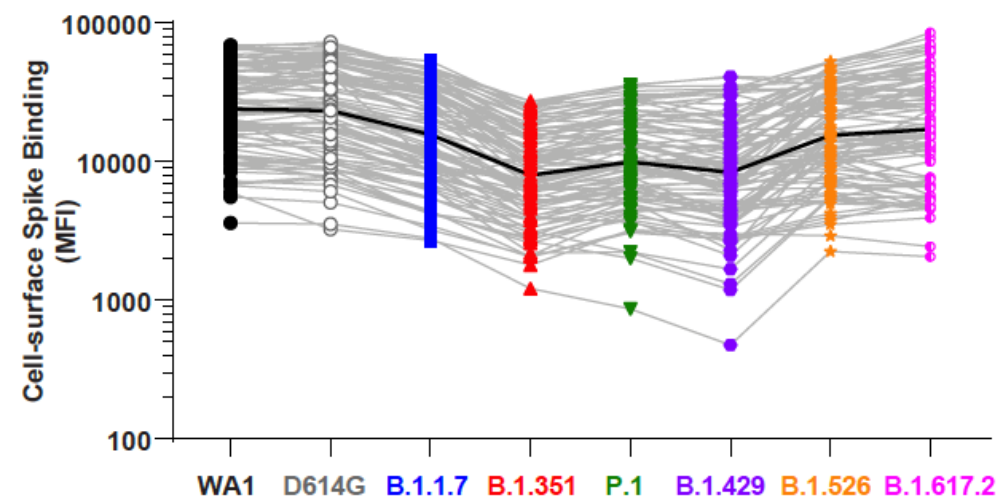
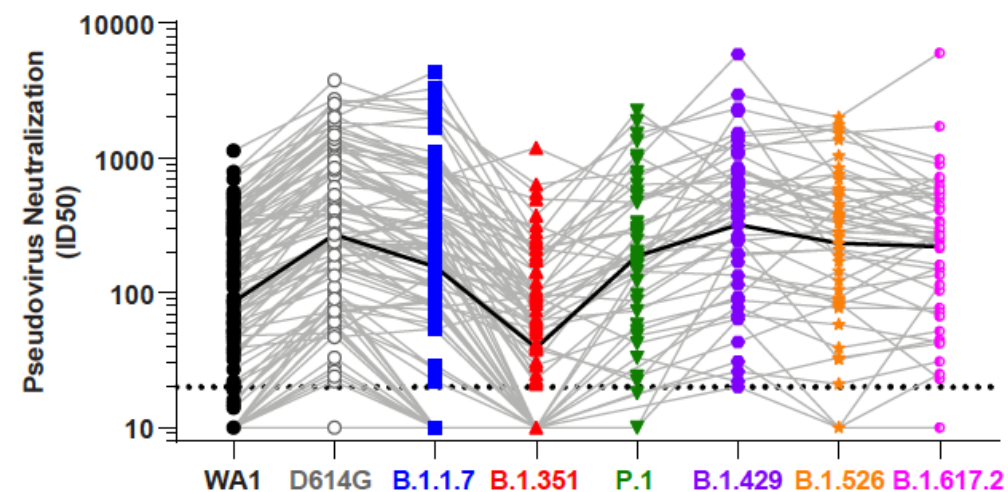
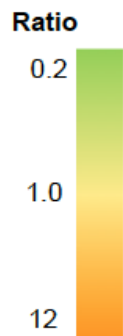
- Low levels 4 weeks after dose 1 (Day 29)
- Peak 2 weeks after dose 2 (Day 43)
- Slow decline over time
- B.1.351 was the worst



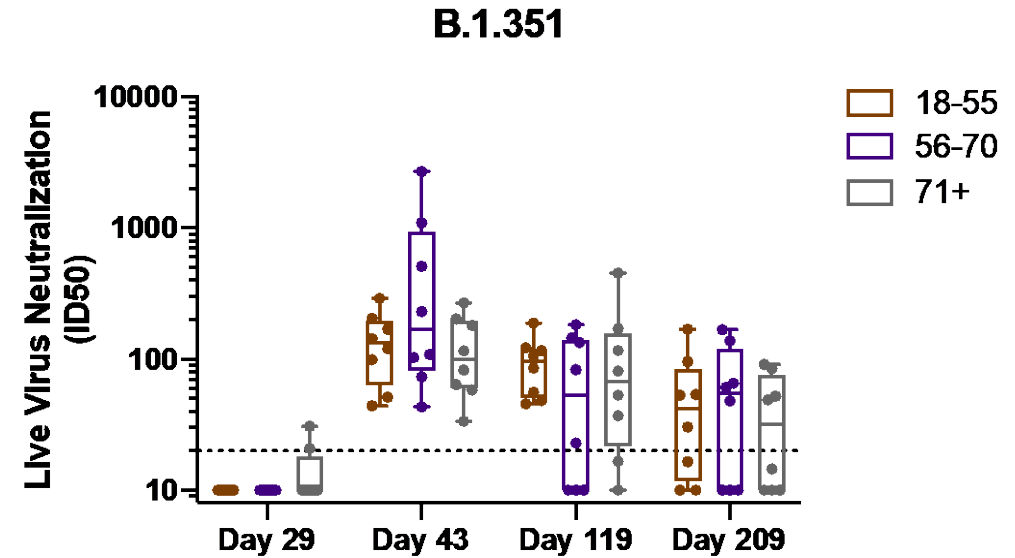
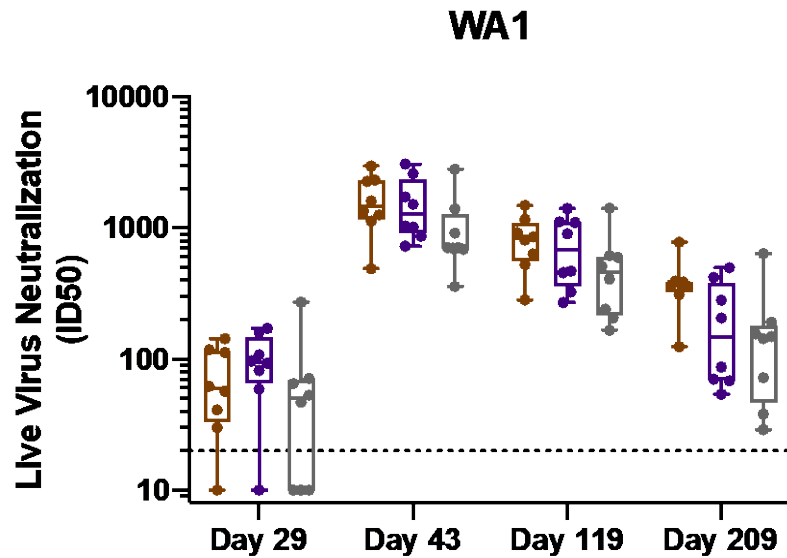


Rank Order of Variants Similar in All Assays

Assay	Variant	Fold reduction Relative To:	
		WA1	D614G
Pseudovirus Neutralization	D614G	0.3	na
	B.1.1.7	0.5	1.7
	B.1.351	2.2	6.9
	P.1	0.9	3.2
	B.1.429	0.5	1.7
	B.1.526	0.7	2.3
	B.1.617.2	0.7	2.4
Live Virus Neutralization	D614G	1.5	na
	B.1.1.7	1.3	1.3
	B.1.351	3.4	4.6
ACE2 Competition	B.1.1.7	3.9	not tested
	B.1.351	11.1	not tested
Cell-Surface Spike Binding	D614G	1.0	na
	B.1.1.7	1.5	1.5
	B.1.351	3.0	2.9
	P.1	2.4	2.4
	B.1.429	2.9	2.8
	B.1.526	1.5	1.5
	B.1.617.2	1.4	1.4
S-2P Binding	B.1.1.7	1.3	not tested
	B.1.351	1.9	not tested
	P.1	1.7	not tested
RBD Binding	B.1.1.7	1.2	not tested
	B.1.351	2.7	not tested
	P.1	1.9	not tested



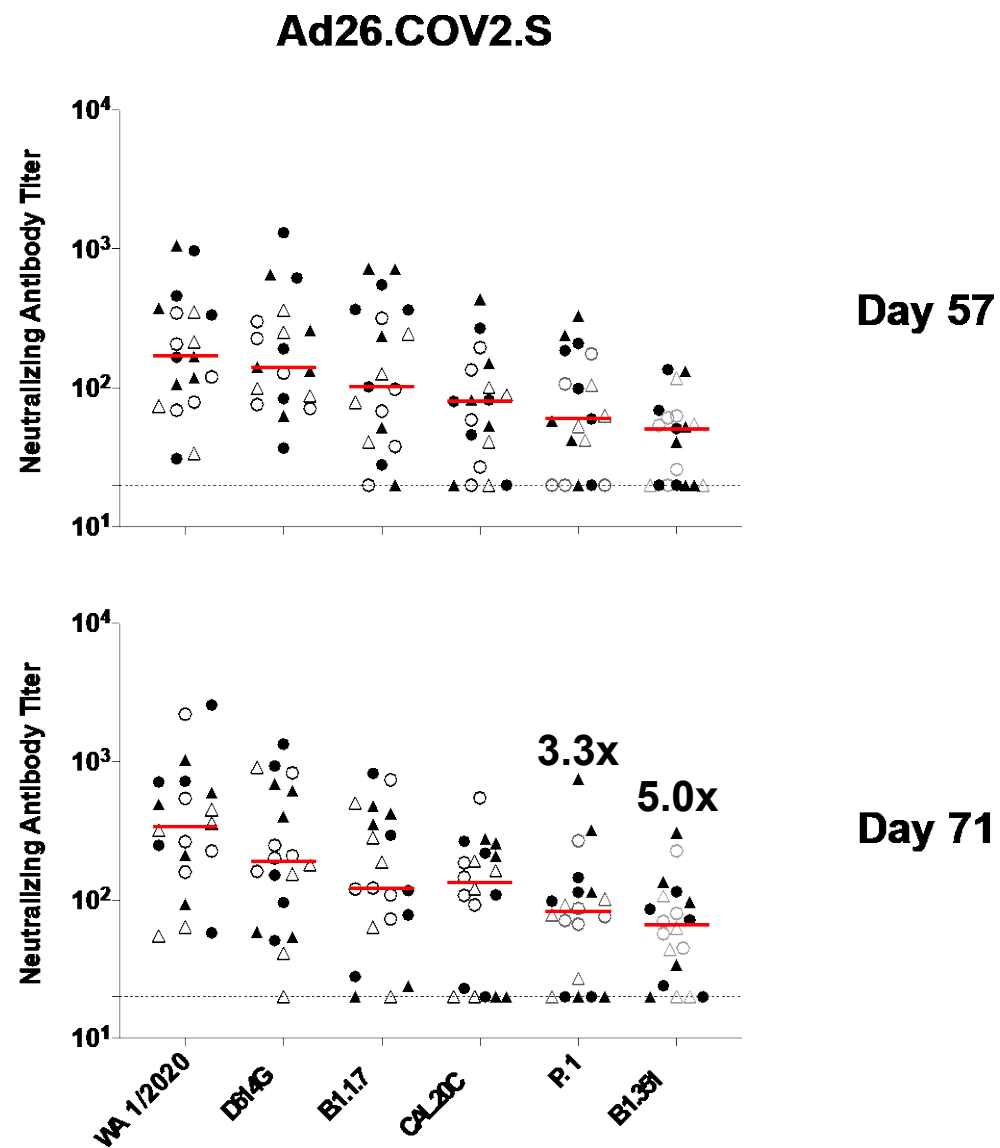
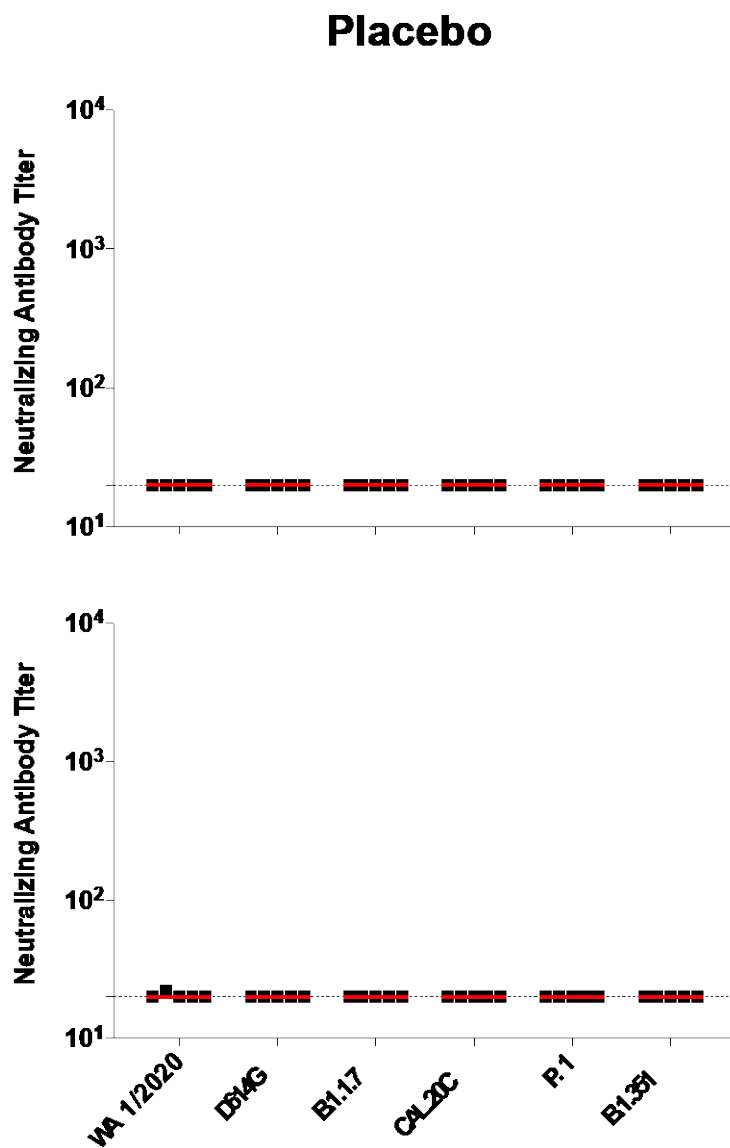
Trend Toward Reduced Durability in the Elderly



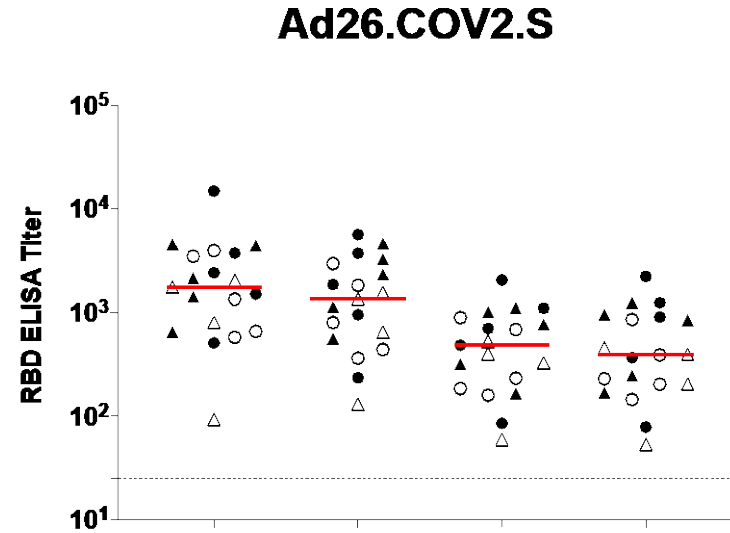
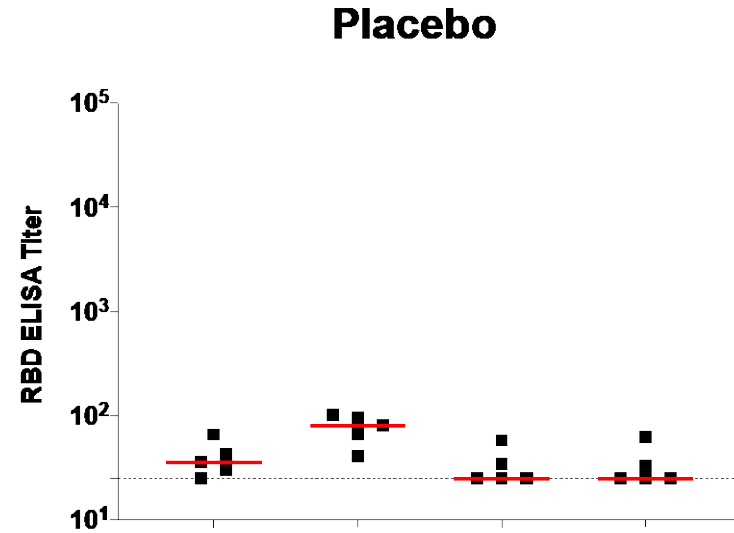
Moderna mRNA-1273: Durability and Coverage of Variants

- Cross-reactive neutralizing responses were rare after a single dose of mRNA-1273
- At the peak of response to the second dose, all subjects had robust responses to all variants
- Binding and functional antibodies against variants persisted in most subjects for 6 months after primary series of mRNA-1273
- Across all assays, B.1.351 had the greatest impact on antibody recognition; B.1.1.7 the least; and P.1, B.1.429, B.1.526, and B.1.617.2 were intermediate
- Trend (marginally statistically significant) to less durability in elderly

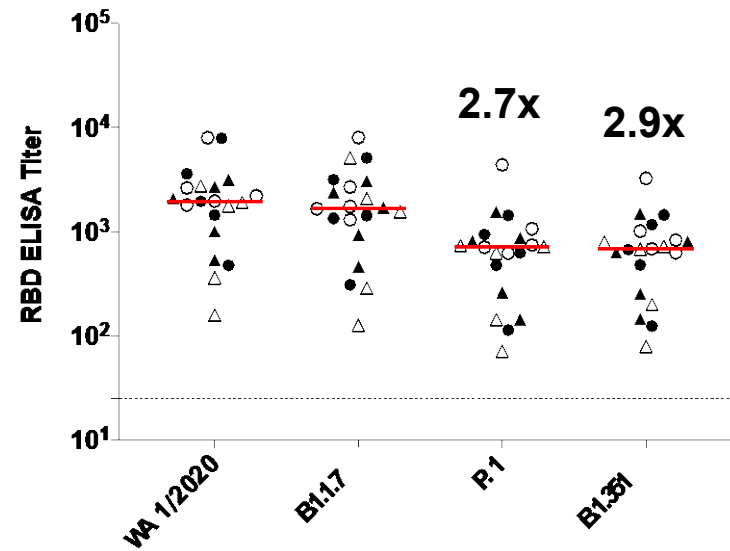
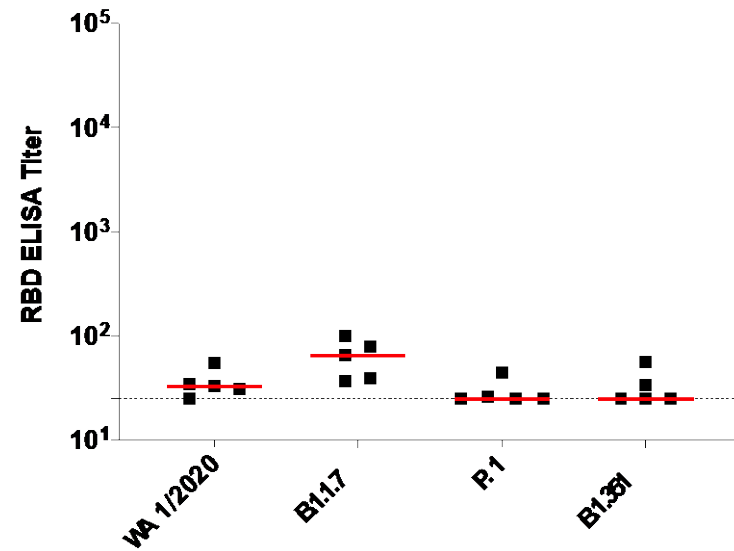
J&J Ad26.COVS.S Neutralization of SARS-CoV-2 Variants



J&J Ad26.COVS.S Binding Antibodies SARS-CoV-2 Variants

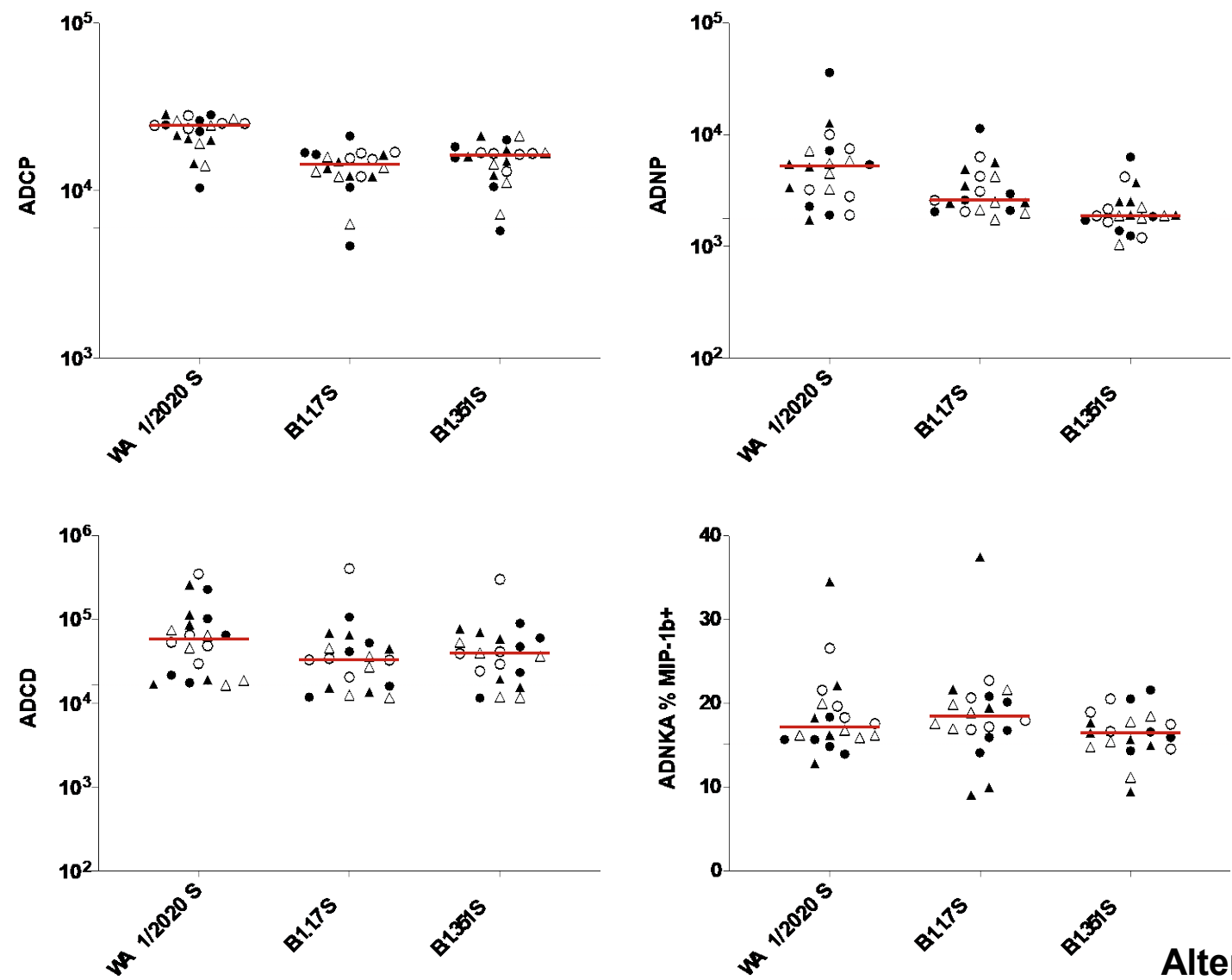


Day 57

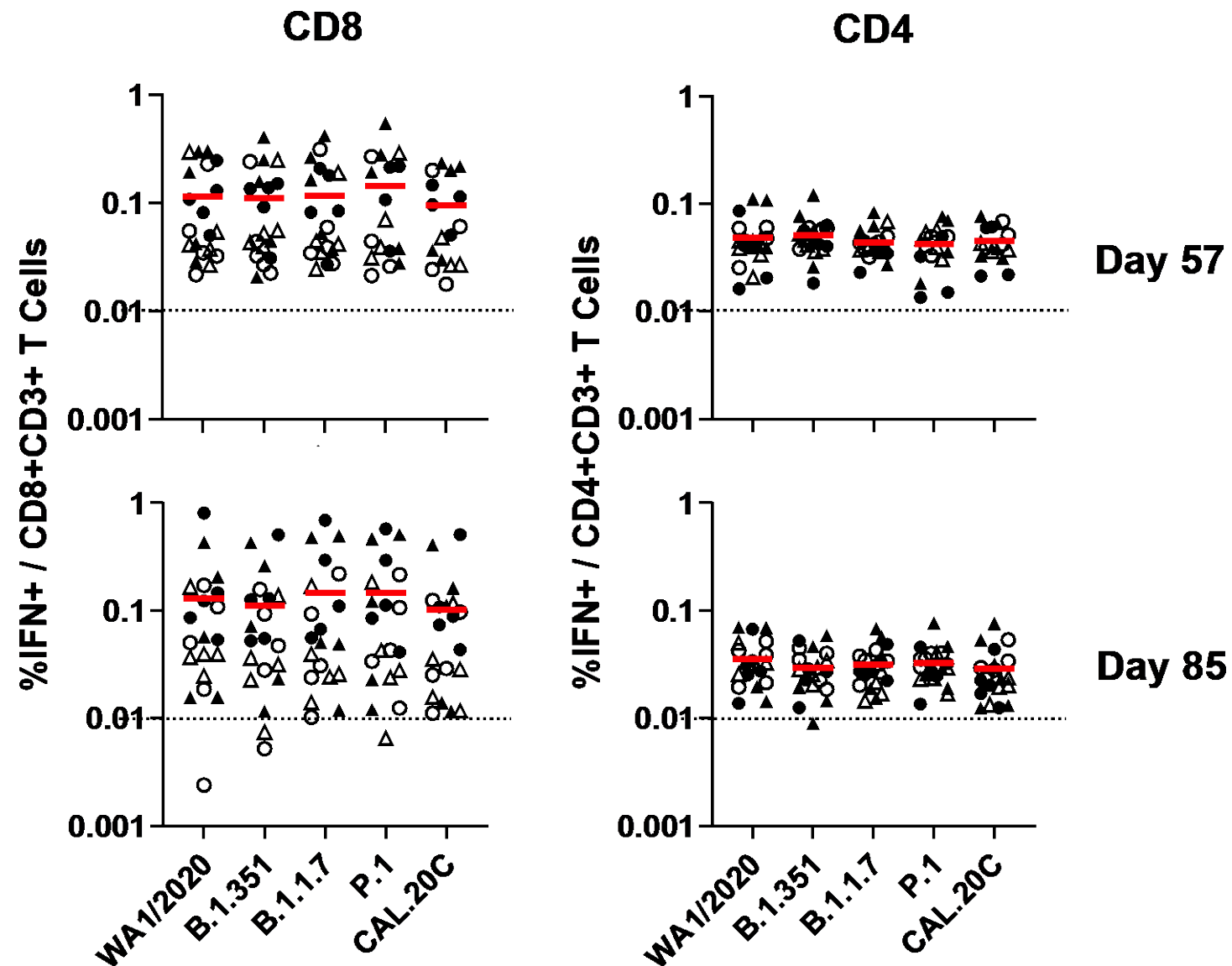


Day 71

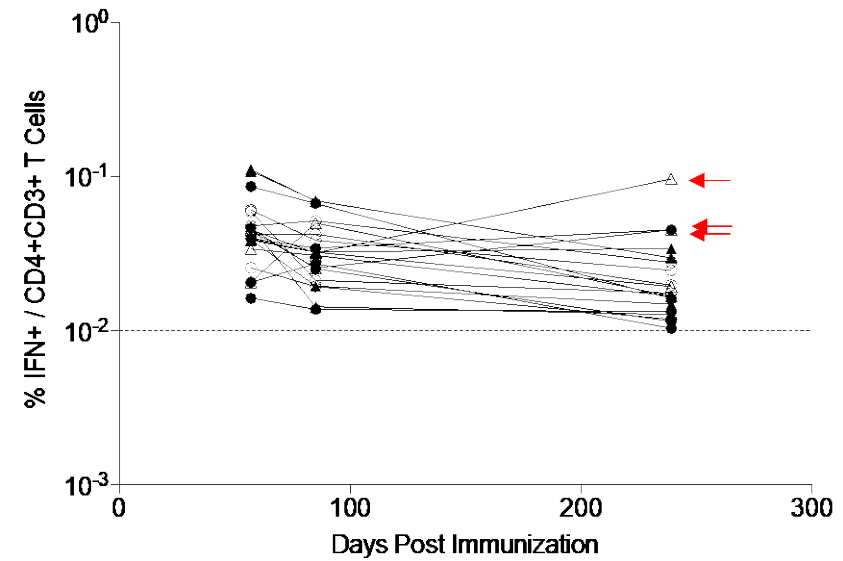
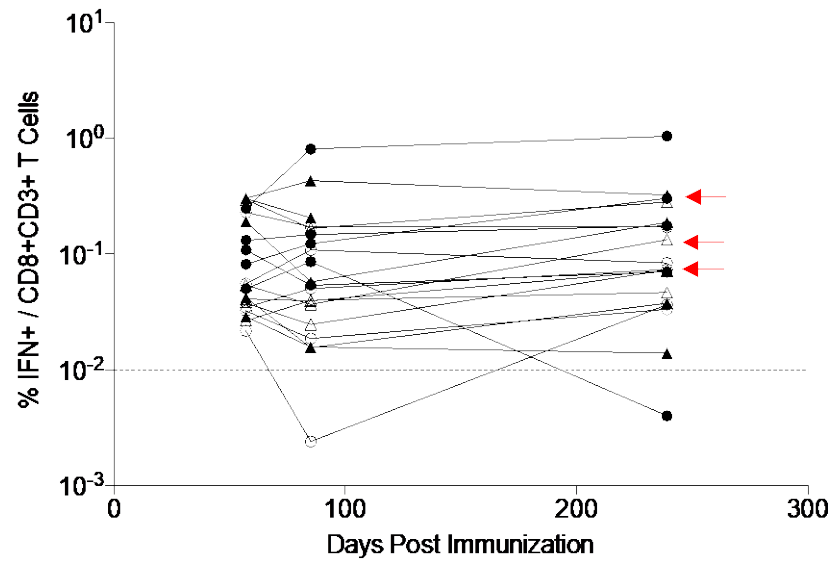
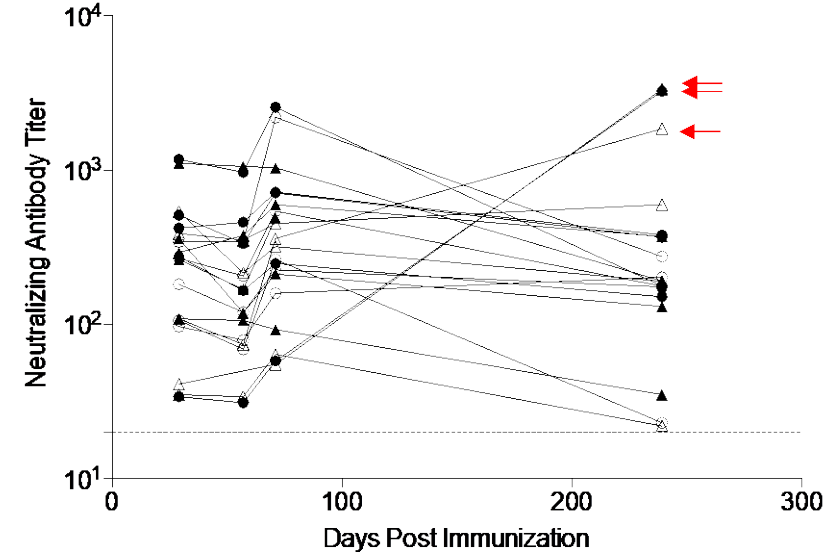
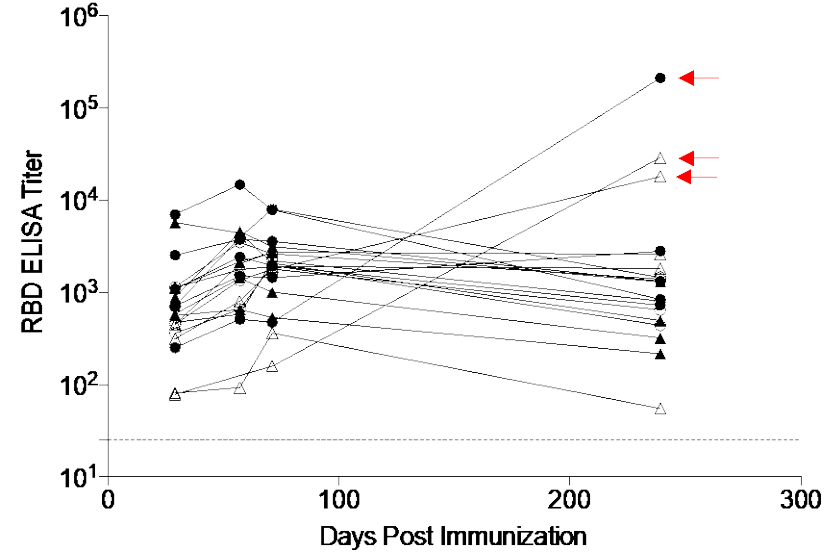
J&J Ad26.COVS.S Fc Functional Antibodies SARS-CoV-2 Variants



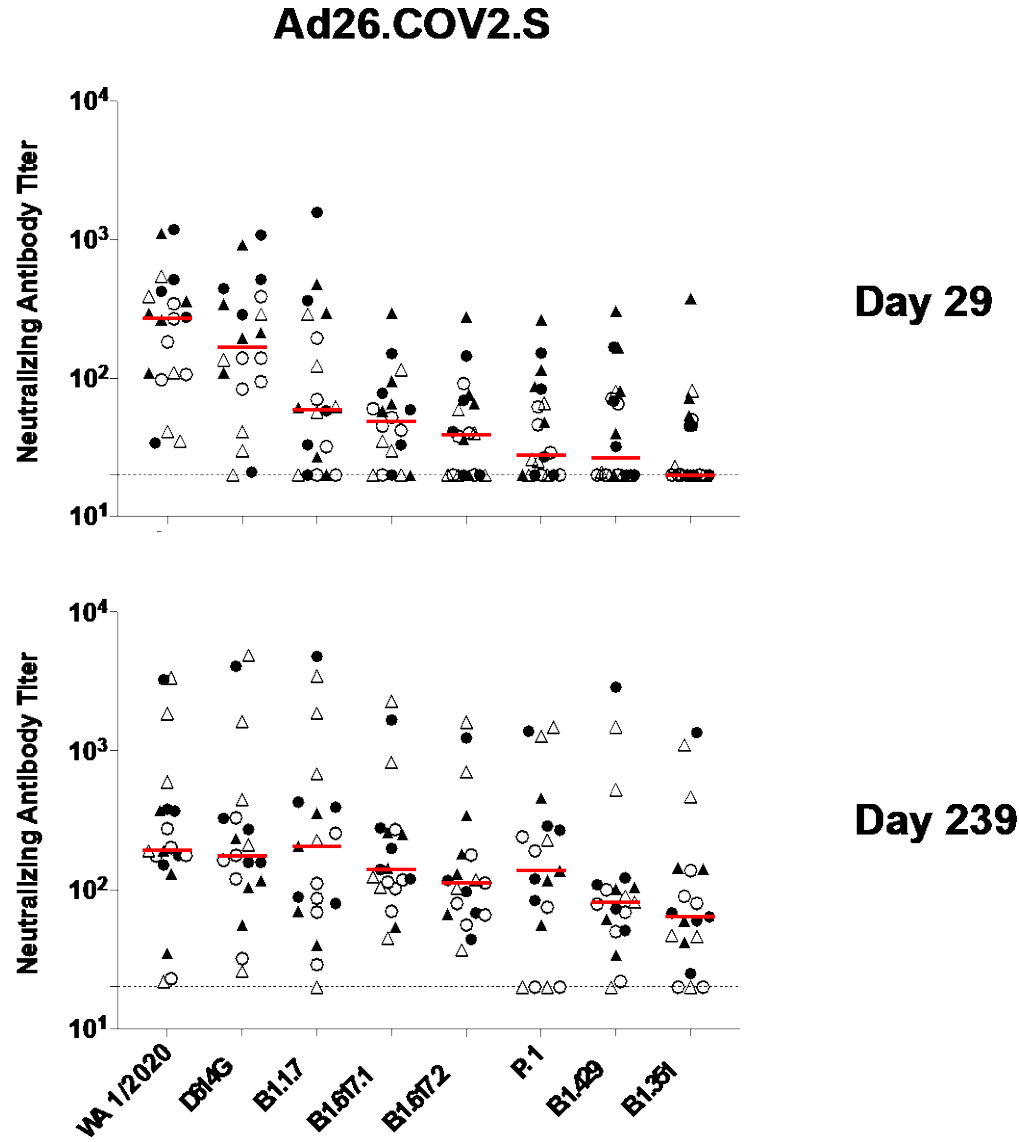
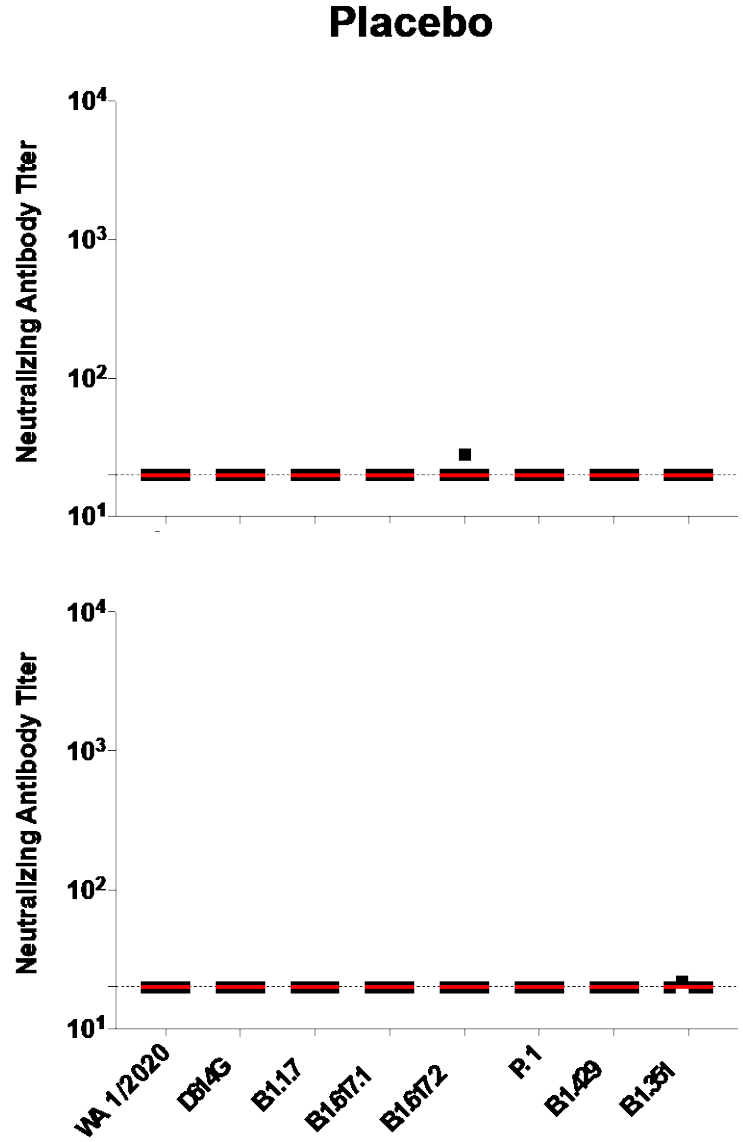
J&J Ad26.COVS.2 S T Cell Responses SARS-CoV-2 Variants



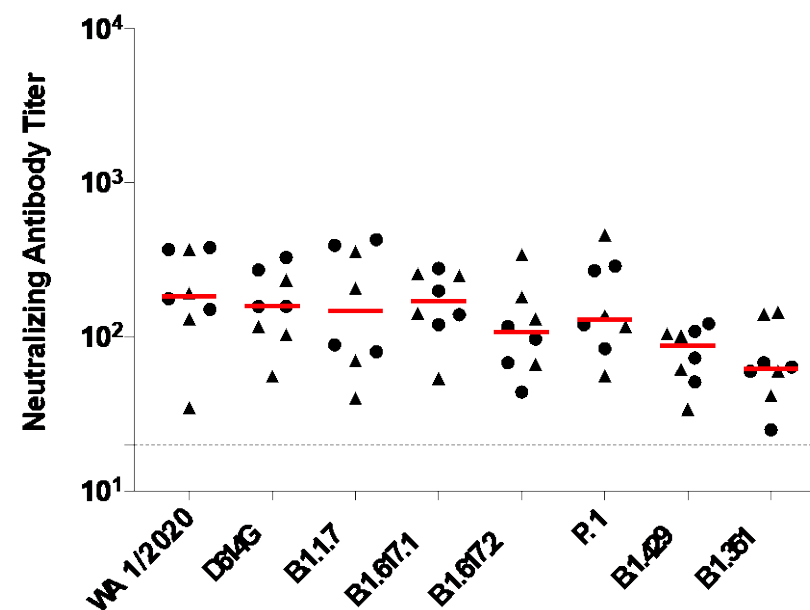
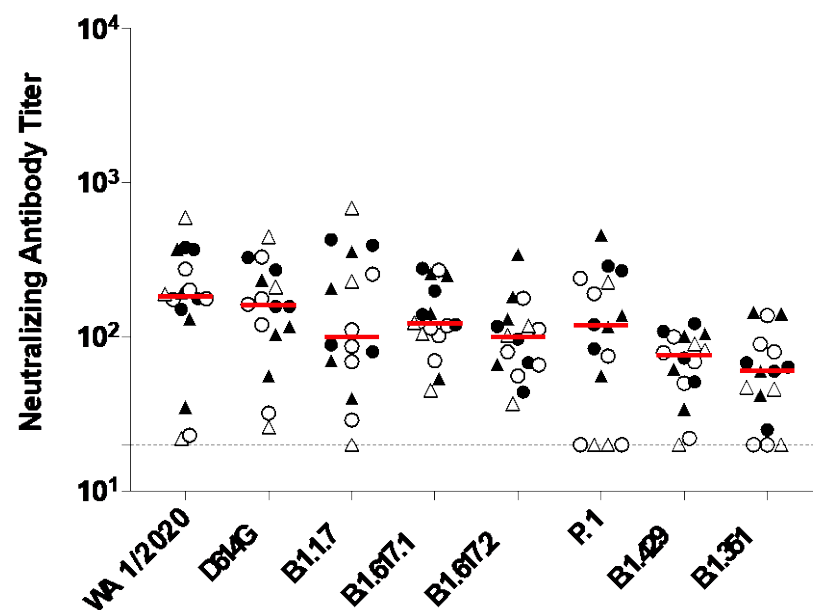
J&J Ad26.COV2.S Durability



J&J Ad26.COV2.S Expansion of Breadth Over Time



J&J Ad26.COV2.S Expansion of Breadth Over Time



J&J Ad26.COV2.S: Durability and Coverage of Variants

- **Reduced neutralizing antibody responses to variants, particularly B.1.351 and less so B.1.617.2**
- **Minimal reductions to Fc functional antibody responses and no reductions to T cell responses to variants**
- **Antibody and T cell responses show minimal decline over 8 months**
- **Neutralizing antibody responses to variants (including delta) appear to increase over time, suggesting B cell maturation even without boosting**

Real World Efficacy Studies Against the Delta Variant

- **Pfizer: Clalit/Israel, Mayo/US, PHE/UK, Qatar**
- **Moderna: Mayo/US, Qatar**
- **J&J: Sisonke/South Africa**
- **All show reduced efficacy against infection and mild disease against the delta variant (some sharply reduced)**
- **All still show high efficacy against severe disease and death**
- **Relative role of declining immunity vs. delta variant remains to be determined**