Component	Reference range	Day 49	Day 89
Lymphocyte count	1.00 – 2.80 X 10^9/l	0.16	1.97
CD3 %	%	49	22
CD3 total	0.70 – 2.10 X 10^9/l	0.08	0.43
CD4 %	%	29	11
CD4 total	0.30 – 1.40 X 10^9/l	0.05	0.22
CD8 %	%	21	10
CD8 total	0.20 – 0.90 X 10^9/l	0.03	0.2
CD19 %	%	21	58
CD19 total	0.10 – 0.50 X 10^9/l	0.03	1.14
CD56 %	%	23	19
CD56 total	0.09 – 0.60 X 10^9/l	0.04	0.37
IgG	6.00 – 16.00 g/l	<1.40	1.9
IgA	0.80 – 4.00 g/l	<0.30	<0.30
IgM	0.50 – 2.00 g/l	1.27	1.92
Sars-CoV-2 Total antibody	(Siemens)	Negative	Positive

Supplemental Table 1: Immunological parameters of patient pre- and post- receipt of convalescent plasma (CP) demonstrating profound lymphopenia with reduction in total serum IgG and IgA. The patient continued to have normal serum IgM which either reflects his underlying lymphoproliferative state or ongoing infection. Following receipt of CP the presence of SARS-CoV-2 antibodies is evident.

Supplementary Table 2. Characteristics of genomes used in the phylogenetic analysis in Figure 2B. Pangolin lineages were identified using Pangolin COVID-19 Lineage Assigner v2.0.8 (https://pangolin.cog-uk.io/).. CP- convalescent plasma; mAb – monoclonal antibody.

Patient	Underlying Clinical Diagnosis	Pangolin Lineage	Treatments
Global GSAID Average	-	-	NA
Choi et al	Antiphospholipid syndrome	B.1	Dual mAb, 3 x remdesivir
Avanzato et al	Chronic lymphocytic leukemia and HLA	A.1	2x CP units
Control patient 1 (purple)	X-linked Agammaglobulinemia	B.2.6	2 x remdesevir, CP after virus clearance
Control Patient 2 (blue)	Chronic renal impairment	B.1.1	None
Control Patient 3 (red)	Heart disease	B.1.1.35	None
Study patient	Marginal B Cell Lymphoma	B.1.1.35/1.1.1	3x CP units, 3 x remdesivir

Timepoint (Day)	sequence	CT value	Sample type	Nanopore	Illumina	SGA
1	NB16_CAMB-1B19D5	25	NT	Y	Y	Y
37	NB23_CAMB-1B4FB2	NA	NT	Y	Y	Y
41	NB01_CAMB-1B5124	23	NT	Y	Y	-
45	NB08_CAMB-1B529A	29	NT	Y	Y	-
50	NB13_CAMB-1B54A3	NA	NT	Y	Y	-
54	NB10_CAMB-1B5643	22	NT	Y	-	-
55	NB08_CAMB-1B5467	NA	NT	Y	Y	Y
56	NB11_CAMB-1B5616	23	NT	Y	-	-
57	NB14_CAMB-1B5607	24	NT	Y	-	-
66	NB05_CAMB-1B55FB	26	NT	Y	Y	-
82	NB06_CAMB-1B55CE	23	NT	Y	Y	-
89	NB01_CAMB-1B5ADE	NA	NT	Y	Y	-
93	NB16_CAMB-1B5BAE	21	NT	Y	Y	-
93	NB17_CAMB-1B5B71	19	ETA	Y	Y	-
95	NB02_CAMB-1B5BCC	16	ETA	Y	Y	-
98	NB01_CAMB-1B5BDB	25	NT	Y	Y	Y
99	NB09_CAMB-1B5C50	30	NT	Y	Y	-
99	NB10_CAMB-1B5C6F	18	ETA	Y	Y	-
100	NB13_CAMB-1B5CE7	NA	NT	Y	Y	-
100	NB14_CAMB-1B5CBA	19	ETA	Y	Y	-
101	NB15_CAMB-1B5CC9	24	ETA	Y	Y	-
101	NB16_CAMB-1B5C9C	30	NT	Y	Y	-

Supplementary table 3 : Samples and sequencing methods. Timepoint indicates the day since 1st positive qPCR for SARS-COV-2 that the sample was taken. CT values are reported where available. Y- Yes, - Not done, NA not available

Supplementary Table 4. Prevalence of selected Spike glycoprotein mutations at sequential time points and sequencing depth (number of reads covering the amino acid position) measured by both short-read (Illumina) and long-read (Oxford Nanopore) methods. There was low coverage of S:P330S and S:D796H in the final three timepoints, measured by both short- and long-read methods.

				Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore
			Day	1	1	37	37	41	41	45	45	50	50	54	54	66	66
Locus	Position	From	To														
2343	NSP2	T	C	0.0%	0.2%	0.0%	0.1%	0.0%	0.2%	0.0%	0.6%	0.0%	0.2%	0.0%	0.9%	100.0%	0.0%
3057	NSP3	A	G	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.2%	0.0%	0.0%	0.0%
5393	NSP3	T	C	0.0%	1.4%	0.2%	0.7%	0.0%	1.1%	0.0%	0.0%	0.2%	1.0%	0.0%	0.9%	0.0%	1.0%
5406	NSP3	T	G	0.0%	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.2%	0.0%	0.0%	0.0%	0.1%	0.0%
5425	NSP3	G	T	0.0%	0.0%	0.0%	0.1%	0.0%	0.1%	0.0%	0.0%	0.0%	0.1%	0.0%	0.1%	0.0%	0.0%
8389	NSP3	C	T	0.0%	0.9%	0.0%	0.4%	0.1%	0.5%	0.0%	0.0%	0.0%	0.9%	0.0%	0.4%	0.0%	0.5%
9130	NSP4	G	T	0.0%	0.1%	0.0%	0.1%	0.0%	0.2%	0.0%	0.0%	0.0%	0.2%	0.0%	0.3%	0.0%	0.4%
10097	NSP5	A	G	30.8%	45.7%	43.6%	56.1%	17.4%	65.1%	23.3%	66.7%	34.0%	46.4%	19.8%	67.8%	18.1%	77.4%
10700	NSP5	G	A	0.0%	0.5%	0.0%	0.7%	0.1%	0.7%	0.0%	0.0%	0.0%	0.7%	0.1%	0.9%	0.0%	0.8%
11770	NSP6	A	G	0.0%	0.7%	0.0%	0.4%	0.1%	0.2%	0.0%	2.2%	0.1%	0.7%	0.0%	0.2%	0.0%	0.4%
12043	NSP7	C	T	0.0%	0.7%	0.1%	0.5%	0.0%	0.7%	0.0%	0.0%	0.1%	0.5%	0.0%	0.9%	0.0%	0.7%
13527	NSP12b	T	C	0.0%	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.0%	0.1%	0.0%	0.1%
14776	NSP12b	G	T	0.0%	0.5%	0.0%	0.3%	0.0%	0.2%	0.1%	0.0%	0.2%	0.1%	0.0%	0.1%	0.1%	0.1%
16733	NSP13	C	T	0.1%	0.2%	2.6%	1.7%	20.9%	13.2%	37.0%	29.8%	0.0%	0.3%	3.6%	1.3%	0.0%	2.0%
17320	NSP13	G	T	0.1%	0.3%	0.3%	0.1%	0.1%	0.2%	0.0%	0.7%	0.0%	0.1%	0.0%	0.0%	0.0%	0.1%
17703	NSP13	C	T	0.0%	0.6%	0.1%	0.8%	0.0%	1.3%	0.0%	1.9%	0.0%	1.5%	0.0%	1.0%	0.0%	1.0%
18488	NSP14a	T	C	0.0%	0.3%	0.0%	0.2%	0.1%	0.4%	0.0%	0.0%	0.0%	0.3%	0.0%	0.2%	0.0%	0.3%
19388	NSP14a	G	A	0.0%	0.0%	0.0%	0.0%	0.0%	0.2%	0.0%	3.1%	0.0%	0.4%	0.0%	0.2%	0.0%	0.5%
20150	NSP15	A	G	0.0%	0.0%	0.0%	0.5%	0.0%	0.2%	0.0%	0.0%	0.2%	0.2%	0.0%	0.8%	0.0%	0.2%
21600	S	G	T	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%	0.1%	0.0%
21635	S	C	A	0.0%	0.0%	0.0%	0.0%	0.0%	0.7%	0.0%	0.0%	0.0%	1.4%	0.0%	0.0%	0.2%	0.8%
21753	S	T	G	0.0%	0.4%	0.0%	0.8%	0.0%	0.0%	0.0%	0.7%	0.0%	0.0%	0.0%	0.4%	0.0%	0.0%
21768	S		-	0.0%	8.4%	0.6%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.0%	4.4%

22088	S	C	T	0.1%	1.0%	0.0%	0.3%	0.0%	0.4%	0.0%	0.0%	0.0%	0.6%	0.5%	0.7%	0.0%	0.9%
22160	S	T	C	0.0%	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%	0.2%
22281	S	C	T	0.1%	0.2%	0.0%	0.1%	0.0%	0.1%	0.0%	0.0%	0.0%	0.1%	0.0%	0.4%	0.0%	0.1%
22551	S	C	T	0.0%	1.1%	0.0%	0.8%	0.0%	0.0%	0.0%	0.7%	0.0%	0.0%	0.1%	1.6%	0.0%	9.0%
23398	S	T	C	0.0%	0.3%	0.0%	0.2%	0.2%	0.1%	0.0%	0.7%	0.0%	0.0%	0.1%	0.1%	0.1%	0.2%
23948	S	G	C	0.0%	0.0%	0.2%	0.0%	0.0%	0.0%	0.1%	0.0%	0.1%	0.0%	2.2%	3.2%	0.2%	1.9%
24257	S	G	T	0.0%	0.0%	0.0%	0.0%	2.1%	2.3%	0.1%	2.7%	27.0%	25.7%	3.3%	0.6%	0.0%	2.6%
25537	E	G	A	0.0%	0.3%	2.6%	2.8%	16.5%	15.4%	20.3%	20.8%	0.1%	0.2%	2.8%	1.0%	0.0%	2.4%
26333	E	C	T	0.0%	0.6%	0.0%	0.1%	0.0%	0.4%	0.0%	0.0%	0.0%	0.2%	0.2%	0.5%	0.0%	0.3%
26634	M	G	T	0.1%	0.4%	0.0%	0.2%	0.0%	0.2%	0.0%	0.8%	0.0%	0.3%	0.0%	0.2%	0.0%	0.2%
26647	M	G	A	0.0%	0.0%	0.0%	0.2%	0.0%	0.2%	0.0%	0.9%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
27087	M	G	A	0.0%	0.6%	0.0%	0.3%	0.1%	0.1%	0.0%	0.0%	0.0%	0.1%	0.0%	0.2%	0.0%	0.1%
27408	ORF7a	T	C	0.0%	0.0%	0.1%	0.0%	0.0%	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%	0.1%
27459	ORF7a	G	T	0.1%	0.4%	0.1%	0.0%	0.1%	0.1%	0.0%	1.4%	0.1%	0.1%	0.0%	0.2%	0.0%	0.4%
27509	ORF7a	C	T	0.0%	0.0%	62.3%	59.8%	44.8%	41.6%	76.7%	65.6%	66.5%	65.3%	24.1%	26.5%	0.0%	22.1%
27618	ORF7a	T	C	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%	0.0%	0.0%	0.0%	0.8%
28209	ORF7b	G	C	0.0%	0.2%	0.0%	0.0%	0.1%	0.1%	0.0%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
28356	N	A	G	0.0%	0.2%	0.3%	0.6%	1.9%	3.0%	0.0%	0.7%	51.0%	48.1%	0.5%	0.5%	0.0%	0.5%
28748	N	C	T	0.0%	0.4%	0.0%	0.1%	0.1%	0.3%	0.0%	0.0%	0.0%	0.3%	0.2%	0.3%	0.0%	0.2%
29825	3'UTR	G	T	0.0%	1.3%	0.2%	0.3%	0.0%	0.6%	0.0%	0.0%	0.2%	0.4%	0.0%	0.2%	0.0%	0.7%

				Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore
			Day	82	82	86	86	89	89	93	93	93	93	95	95	98	98
Locus	Position	From	To														
2343	NSP2	T	C	0.0%	0.1%	97.6%	2.2%	91.1%	98.5%	0.1%	0.2%	2.1%	95.5%	19.4%	90.7%	15.0%	0.4%
3057	NSP3	A	G	0.0%	0.1%	0.0%	0.0%	0.0%	0.1%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.7%	0.1%
5393	NSP3	T	C	0.2%	1.3%	0.4%	0.9%	0.0%	1.3%	0.2%	1.2%	0.0%	1.3%	7.4%	1.2%	78.8%	1.2%
5406	NSP3	T	G	0.0%	0.0%	29.3%	0.1%	66.5%	0.0%	0.3%	0.1%	2.3%	15.8%	17.4%	56.2%	10.9%	0.3%
5425	NSP3	G	T	99.9%	0.3%	0.9%	0.0%	9.0%	0.0%	0.0%	97.4%	0.6%	0.5%	7.4%	7.9%	82.6%	0.2%
8389	NSP3	C	T	0.0%	0.7%	0.0%	0.3%	0.0%	0.3%	20.6%	0.5%	19.6%	0.7%	22.2%	0.4%	0.1%	21.9%
9130	NSP4	G	T	0.0%	0.4%	0.0%	0.2%	0.0%	0.3%	0.1%	0.3%	0.0%	0.3%	0.0%	0.3%	12.6%	0.4%
10097	NSP5	A	G	41.8%	74.4%	17.2%	82.3%	9.5%	70.0%	21.5%	49.0%	13.9%	64.3%	12.4%	73.6%	20.9%	73.7%
10700	NSP5	G	A	0.0%	0.4%	0.0%	0.6%	0.3%	0.8%	99.5%	0.6%	96.8%	0.6%	76.9%	0.5%	0.1%	98.8%
11770	NSP6	A	G	0.1%	0.5%	0.3%	0.4%	0.1%	0.4%	97.9%	0.3%	90.4%	0.4%	73.1%	0.3%	0.1%	96.8%
12043	NSP7	C	T	0.0%	1.1%	20.1%	0.4%	51.1%	0.6%	0.2%	0.7%	3.3%	20.7%	13.0%	53.3%	13.3%	0.6%
13527	NSP12b	T	C	0.0%	0.2%	0.3%	0.1%	0.4%	0.0%	57.3%	0.0%	52.1%	0.1%	34.8%	0.1%	0.0%	54.6%
14776	NSP12b	G	T	0.1%	0.2%	0.2%	0.1%	0.0%	0.1%	54.1%	0.3%	50.7%	0.6%	34.6%	0.2%	0.0%	57.7%
16733	NSP13	C	T	0.0%	5.0%	0.0%	2.6%	0.0%	0.2%	0.0%	0.1%	0.0%	0.2%	0.0%	0.2%	0.4%	0.1%
17320	NSP13	G	T	0.0%	0.1%	0.5%	0.0%	0.0%	0.1%	0.0%	0.1%	0.0%	0.5%	0.0%	0.2%	1.0%	0.1%
17703	NSP13	C	T	0.0%	1.4%	0.0%	1.5%	0.0%	0.8%	15.5%	1.4%	9.0%	1.0%	17.4%	1.1%	0.0%	16.1%
18488	NSP14a	T	C	0.0%	0.2%	0.0%	0.2%	0.0%	0.4%	16.2%	0.2%	8.5%	0.3%	18.3%	0.3%	0.0%	15.7%
19388	NSP14a	G	A	0.0%	0.2%	0.0%	0.2%	0.0%	0.2%	17.8%	0.5%	11.9%	0.7%	20.9%	0.0%	0.0%	17.4%
20150	NSP15	A	G	0.0%	0.4%	92.8%	0.6%	92.6%	0.1%	0.6%	0.7%	1.9%	94.9%	16.5%	90.8%	18.3%	0.7%
21600	S	G	T	0.0%	0.0%	0.0%	0.0%	0.3%	0.0%	99.2%	0.0%	97.1%	0.0%	76.3%	0.0%	0.7%	99.1%
21635	S	C	A	0.0%	0.5%	0.0%	0.0%	0.2%	1.3%	27.9%	0.8%	14.6%	0.4%	23.5%	0.0%	0.0%	26.8%
21753	S	T	G	0.0%	0.7%	0.0%	0.8%	0.0%	0.5%	96.5%	80.2%	0.0%	0.0%	62.7%	60.3%	0.0%	0.3%
21768	S		-	99.0%	93.0%	0.0%	6.9%	6.0%	1.0%	0.0%	9.2%	0.0%	0.0%	12.0%	10.4%	82.6%	93.5%
22088	S	C	T	0.1%	0.9%	0.0%	0.9%	0.0%	1.1%	15.6%	1.1%	6.4%	2.8%	16.8%	1.2%	0.0%	6.8%
22160	S	T	C	0.1%	0.0%	82.7%	0.0%	86.5%	0.0%	0.6%	0.1%	0.9%	68.7%	13.8%	85.6%	8.1%	0.6%
22281	S	C	T	0.1%	0.3%	82.7%	0.2%	84.5%	0.1%	0.4%	0.2%	1.8%	54.0%	11.1%	73.3%	6.3%	0.3%
22551	S	C	T	0.0%	0.9%	0.0%	0.9%	0.0%	0.9%	96.9%	92.8%	0.0%	0.0%	78.3%	73.3%	0.0%	1.3%

23398	S	T	C	0.1%	0.0%	24.9%	0.0%	65.9%	0.1%	0.4%	0.1%	2.2%	22.1%	16.2%	62.1%	12.7%	0.4%
23948	S	G	C	99.8%	2.3%	2.8%	4.8%	8.7%	0.0%	0.2%	99.2%	0.2%	2.9%	6.5%	8.7%	79.1%	0.1%
24257	S	G	T	0.0%	0.4%	0.0%	0.3%	0.0%	0.4%	0.0%	0.3%	0.0%	0.1%	0.0%	0.2%	0.0%	0.0%
25537	E	G	A	0.0%	3.5%	0.0%	1.4%	0.0%	0.1%	0.0%	0.1%	0.0%	0.1%	0.0%	0.2%	0.0%	0.1%
26333	E	C	T	0.0%	0.5%	0.0%	0.2%	0.2%	0.2%	99.3%	0.5%	97.6%	0.3%	77.9%	0.1%	0.0%	97.8%
26634	M	G	T	0.1%	0.2%	0.1%	0.2%	0.0%	0.1%	43.0%	0.3%	31.8%	0.2%	10.6%	0.2%	0.0%	40.2%
26647	M	G	A	0.0%	0.1%	0.0%	0.1%	0.0%	0.1%	22.5%	0.1%	27.6%	0.1%	6.5%	0.1%	0.0%	18.5%
27087	M	G	A	0.1%	0.3%	0.0%	0.2%	0.0%	0.1%	16.4%	0.3%	10.7%	0.3%	18.2%	0.2%	0.0%	18.6%
27408	ORF7a	T	C	0.0%	0.1%	28.2%	0.0%	64.1%	0.0%	0.3%	0.1%	2.5%	23.3%	14.0%	49.5%	10.0%	0.3%
27459	ORF7a	G	T	0.2%	0.3%	0.0%	0.7%	2.6%	0.1%	0.1%	0.3%	0.1%	0.0%	4.1%	3.5%	66.9%	0.2%
27509	ORF7a	C	T	0.0%	27.3%	0.0%	10.8%	0.0%	0.6%	0.0%	0.5%	0.4%	0.4%	0.1%	0.1%	0.2%	0.5%
27618	ORF7a	T	C	0.1%	0.0%	0.0%	0.0%	1.4%	0.0%	99.5%	0.3%	97.4%	0.0%	85.6%	0.0%	0.8%	97.5%
28209	ORF7b	G	C	0.0%	0.0%	0.0%	0.0%	0.7%	0.0%	0.2%	0.0%	1.5%	0.0%	12.4%	0.6%	3.1%	0.3%
28356	N	A	G	99.9%	0.6%	2.3%	0.6%	6.1%	0.6%	0.2%	98.3%	0.2%	2.7%	5.9%	6.6%	78.6%	0.6%
28748	N	C	T	0.0%	0.4%	2.2%	0.2%	0.0%	0.3%	0.1%	0.3%	1.7%	2.6%	12.9%	0.1%	2.8%	0.4%
29825	3'UTR	G	T	99.8%	0.5%	4.7%	0.4%	8.7%	0.1%	0.3%	98.5%	0.5%	3.0%	6.4%	9.4%	80.5%	0.7%

				Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore	Illumina	Nanopore
			Day	99	99	99	99	100	100	100	100	101	101	101	101
Locus	Position	From	To												
2343	NSP2	T	C	18.2%	81.4%	5.4%	67.1%	0.0%	0.4%	2.8%	11.9%	7.8%	3.1%	0.0%	0.6%
3057	NSP3	A	G	0.0%	2.4%	38.4%	14.5%	29.0%	13.1%	32.4%	0.2%	29.7%	28.6%	0.0%	28.2%
5393	NSP3	T	C	14.4%	0.0%	0.0%	0.0%	10.4%	0.1%	0.0%	12.3%	0.0%	0.0%	0.0%	9.5%
5406	NSP3	T	G	46.4%	1.4%	65.3%	7.4%	30.8%	77.0%	65.3%	39.3%	65.2%	65.5%	16.0%	30.8%
5425	NSP3	G	T	0.0%	1.4%	29.8%	10.7%	25.7%	7.0%	29.9%	0.0%	27.9%	19.4%	0.0%	20.2%
8389	NSP3	C	T	96.4%	0.2%	65.6%	5.2%	53.6%	79.5%	65.5%	97.8%	64.4%	60.8%	98.9%	42.4%
9130	NSP4	G	T	0.0%	16.9%	1.3%	21.9%	0.0%	0.3%	0.6%	0.0%	1.4%	1.1%	0.0%	0.7%
10097	NSP5	A	G	15.8%	0.1%	0.0%	0.3%	19.7%	10.9%	0.0%	16.0%	0.0%	0.3%	0.0%	18.9%
10700	NSP5	G	A	1.7%	63.8%	87.6%	73.1%	16.7%	67.0%	17.9%	87.5%	25.6%	9.7%	0.0%	58.9%
11770	NSP6	A	G	12.2%	96.9%	4.4%	79.1%	0.1%	0.8%	3.3%	13.6%	5.6%	4.8%	0.1%	0.7%
12043	NSP7	C	T	44.1%	93.2%	5.2%	78.4%	0.5%	0.2%	3.3%	44.2%	5.5%	4.4%	0.2%	0.4%
13527	NSP12b	T	C	0.0%	2.6%	27.6%	15.1%	13.0%	12.1%	26.0%	0.9%	27.6%	27.9%	18.7%	12.9%
14776	NSP12b	G	T	1.4%	50.2%	1.5%	32.6%	0.0%	0.2%	1.0%	1.3%	3.3%	2.3%	0.0%	0.0%
16733	NSP13	C	T	0.0%	51.4%	2.3%	31.3%	0.1%	0.2%	1.5%	0.0%	1.8%	0.9%	0.0%	0.0%
17320	NSP13	G	T	0.0%	0.1%	0.0%	0.2%	0.0%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
17703	NSP13	C	T	0.0%	0.1%	0.2%	0.1%	19.0%	1.1%	0.0%	0.1%	0.1%	0.2%	14.2%	18.9%
18488	NSP14a	T	C	0.0%	9.7%	0.7%	17.1%	0.0%	1.2%	1.0%	0.0%	0.8%	2.0%	0.0%	1.7%
19388	NSP14a	G	A	0.0%	7.6%	1.0%	16.3%	0.0%	0.4%	0.2%	0.0%	0.6%	1.3%	0.0%	0.2%
20150	NSP15	A	G	0.0%	9.8%	0.9%	20.0%	0.0%	1.0%	1.0%	0.0%	1.6%	1.4%	0.0%	0.0%
21600	S	G	T	0.0%	2.0%	31.6%	16.8%	45.1%	17.1%	35.5%	0.0%	28.6%	31.3%	2.1%	40.9%
21635	S	C	A	12.1%	96.5%	16.9%	78.6%	0.0%	0.4%	18.9%	20.0%	6.1%	0.0%	0.0%	0.0%
21753	S	T	G	0.0%	20.2%	5.3%	23.4%	0.0%	0.7%	12.2%	7.7%	0.0%	0.0%	0.0%	0.0%
21768	S		-	0.0%	3.6%	0.0%	0.0%	0.0%	3.1%	0.0%	0.0%	0.0%	0.7%	0.0%	0.0%
22088	S	C	T	67.7%	90.0%	0.0%	0.0%	70.3%	96.5%	0.0%	0.0%	86.3%	91.0%	0.0%	0.0%
22160	S	T	C	0.0%	3.0%	0.0%	5.9%	0.0%	1.4%	0.0%	0.0%	0.2%	0.0%	0.0%	6.3%
22281	S	C	T	9.1%	1.4%	0.0%	13.9%	23.9%	8.1%	35.7%	0.0%	28.2%	16.7%	0.8%	33.3%
22551	S	C	T	5.7%	1.0%	0.0%	10.7%	26.7%	8.0%	6.1%	0.0%	26.6%	3.0%	0.8%	35.0%

23398	S	T	C	20.0%	0.0%	0.0%	0.0%	0.0%	4.8%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
23948	S	G	C	0.0%	1.8%	36.9%	13.0%	35.1%	10.0%	30.5%	0.0%	26.6%	28.5%	0.1%	28.1%
24257	S	G	T	82.7%	0.0%	58.0%	6.8%	72.2%	81.2%	71.8%	85.6%	66.5%	70.8%	100.0%	76.7%
25537	E	G	A	0.0%	0.7%	0.0%	0.2%	10.1%	0.3%	0.0%	0.0%	0.1%	0.2%	0.0%	7.4%
26333	E	C	T	0.0%	0.3%	0.0%	0.1%	0.0%	0.3%	0.0%	0.1%	0.0%	0.1%	0.0%	0.0%
26634	M	G	T	38.6%	96.3%	0.9%	76.9%	0.0%	0.1%	3.7%	40.9%	7.9%	7.7%	0.0%	1.0%
26647	M	G	A	1.8%	30.9%	0.2%	9.2%	0.0%	0.4%	0.0%	2.0%	0.6%	0.4%	0.0%	0.0%
27087	M	G	A	0.0%	25.4%	0.2%	5.3%	0.0%	0.1%	0.1%	0.1%	0.0%	0.4%	0.1%	0.0%
27408	ORF7a	T	C	10.0%	10.9%	1.0%	19.4%	0.0%	0.2%	0.8%	7.6%	1.2%	0.9%	0.0%	0.0%
27459	ORF7a	G	T	6.4%	2.0%	29.7%	10.3%	16.9%	7.1%	32.3%	3.6%	26.9%	22.5%	0.0%	14.0%
27509	ORF7a	C	T	76.5%	0.4%	64.1%	6.9%	50.5%	74.7%	59.6%	80.9%	54.6%	65.1%	79.7%	55.9%
27618	ORF7a	T	C	0.1%	0.3%	0.0%	0.5%	1.2%	0.5%	0.1%	0.3%	0.8%	0.3%	0.0%	1.9%
28209	ORF7b	G	C	33.3%	96.4%	34.8%	82.8%	0.0%	0.0%	7.2%	0.0%	13.0%	0.0%	0.0%	0.0%
28356	N	A	G	0.0%	1.8%	25.7%	13.2%	1.3%	2.6%	28.5%	0.1%	27.5%	25.0%	0.0%	0.8%
28748	N	C	T	87.9%	0.6%	55.1%	7.2%	50.0%	78.6%	58.9%	86.5%	56.4%	59.0%	94.6%	45.0%
29825	3'UTR	G	T	0.0%	2.4%	26.1%	13.5%	0.1%	3.3%	27.7%	0.0%	26.4%	30.6%	0.0%	0.5%

Supplementary Table 5: Single genome sequencing (SGS) data from respiratory samples at indicated days. Indicated are the number of single genomes obtained at each time point with the mutations of interest (identified by deep sequencing). *denominator is 19 as for 2 samples the primer reads were poor quality at amino acid 796 at day 98.

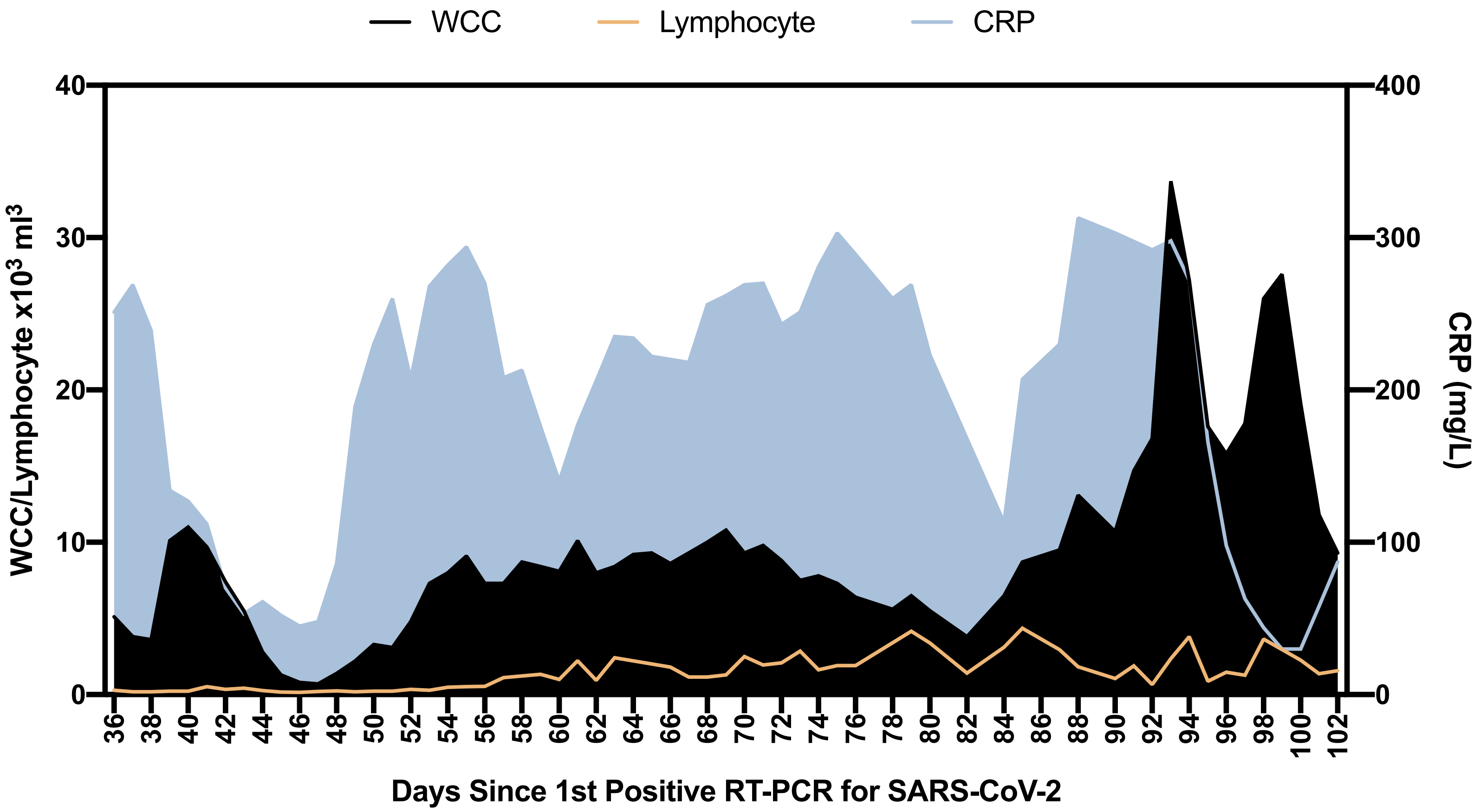
	W64G	P330S	69/70	D796H	T200I	Y240H
Day 1 (n=7)	0	0	0	0	0	0
Day 37 (n=38)	0	0	0	0	0	0
Day 98 (n=21)	1 (4.8%)	1 (4.8%)	17 (81.0%)	13*(68.4%)	3 (14.3%)	3 (14.3%)

Supplementary table 6: Neutralisation of mutants by *Seven RBD-specific mAbs (from Bauwer et al. in Figure 7).* Clusters II, V contain only non-neutralising mAbs, smaller neutralising mAb clusters IV (n=2) and X (n=1) were not tested. Red indicates significant fold changes.

mAb	Cluster	Target		WT	D796H	Δ6970	Δ6970-D796H	Fold decrease		
COVA1-18	I	RBD		0.0014	0.0022	0.0016	0.0013	1.6	1.2	1.0
COVA2-39	I	RBD	Structure	0.0143	0.0203	0.0319	0.0163	1.4	2.2	1.1
COVA1-16	III	RBD	Structure	0.2441	0.1242	0.2651	0.1308	0.5	1.1	0.5
COVA2-07	III	RBD		0.0349	0.0269	0.0288	0.0272	0.8	0.8	0.8
COVA2-04	III	RBD	Structure	0.2887	0.1009	0.2425	0.1401	0.3	0.8	0.5
COVA2-17	IX	RBD		0.0156	0.0248	0.0139	0.0113	1.6	0.9	0.7
COVA2-02	VII	RBD		5.8590	4.9670	6.5680	3.5380	0.8	1.1	0.6
COVA1-12	VI	RBD		0.2007	0.1863	0.1105	0.0611	0.9	0.6	0.3
COVA1-21	XI	Non-RBD		0.1189	0.0498	0.6035	0.5682	0.4	5.1	4.8

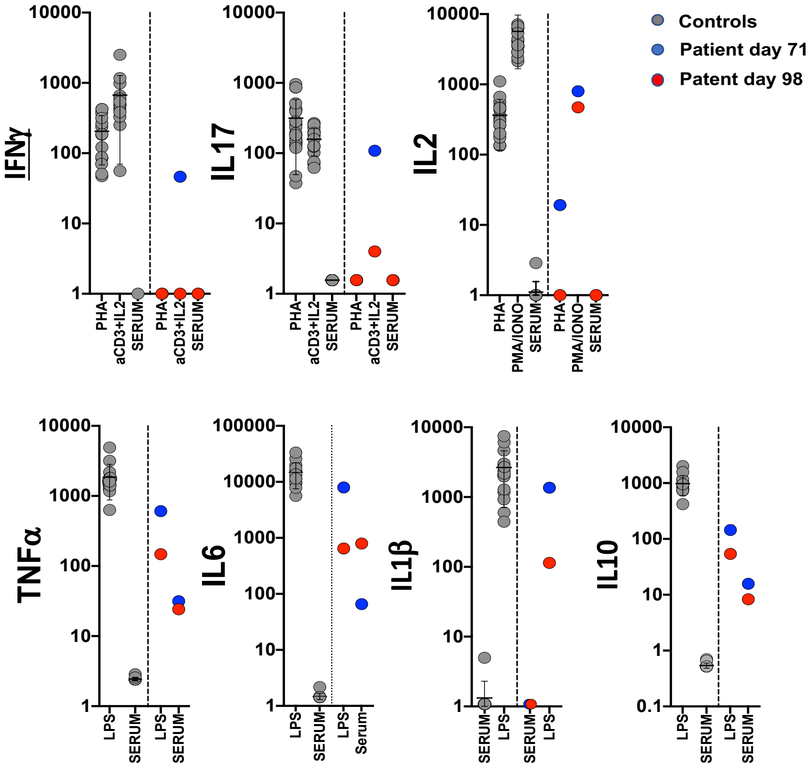
Supplementary Table 7. Global prevalence of selected spike mutations detailed in this paper. All high coverage sequences were downloaded from the GISAID database on 11th November and aligned using MAFFT. The global prevalence of each of the six spike mutations W64G, ΔH69/V70, Y200H, T240I, P330S and D796H were assessed by viewing the multiple sequence alignment in AliView, sorting by the column of interest, and counting the number of mutations.

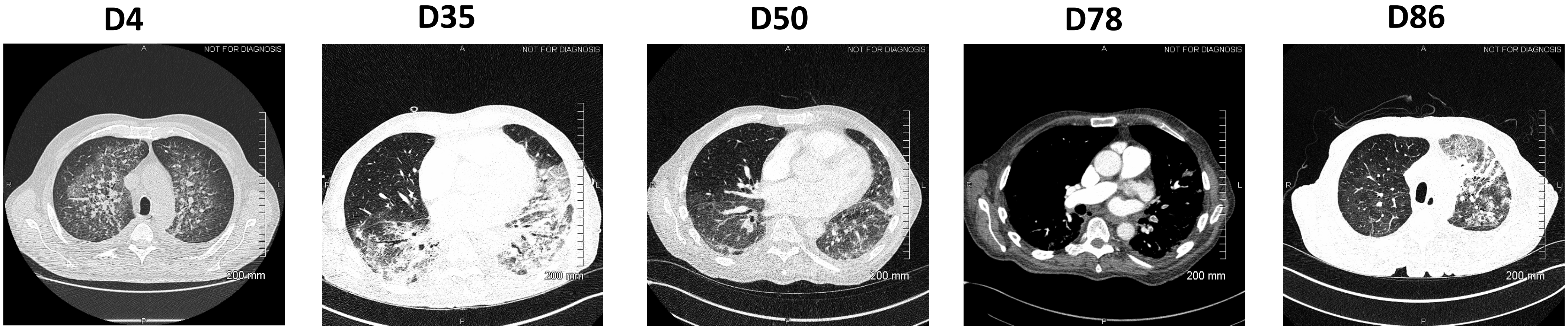
Mutation	Number of Sequences	Global Prevalence
W64G	0	0.00%
ΔH69/V70	2920	1.38%
Y200H	7	0.00%
T240I	34	0.02%
P330S	130	0.06%
D796H	25	0.01%



Supplementary Figure 1: Blood parameters over time in patient case: White cell count (WCC) and lymphocyte counts are expressed as x10^3 Cells/mm^3. CRP: C reactive protein

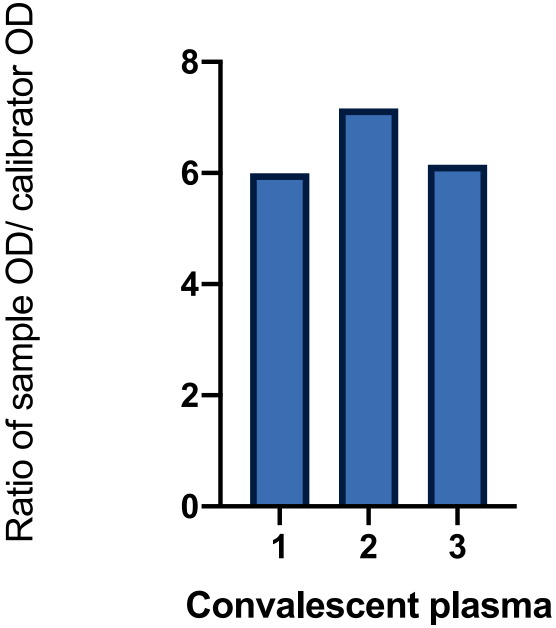
Supplementary Figure 2: Assessment of T cell and innate function. Whole blood cytokines were measured in whole blood after 24 hours stimulation either after T-cell stimulation with PHA or anti CD3/IL2 or innate stimulation with LPS . Healthy controls are shown as grey circles (N=15), Patient at d71 and d98 is shown as blue circles or red circles respectively. Cytokine levels are shown as pg/ml. stimulation.

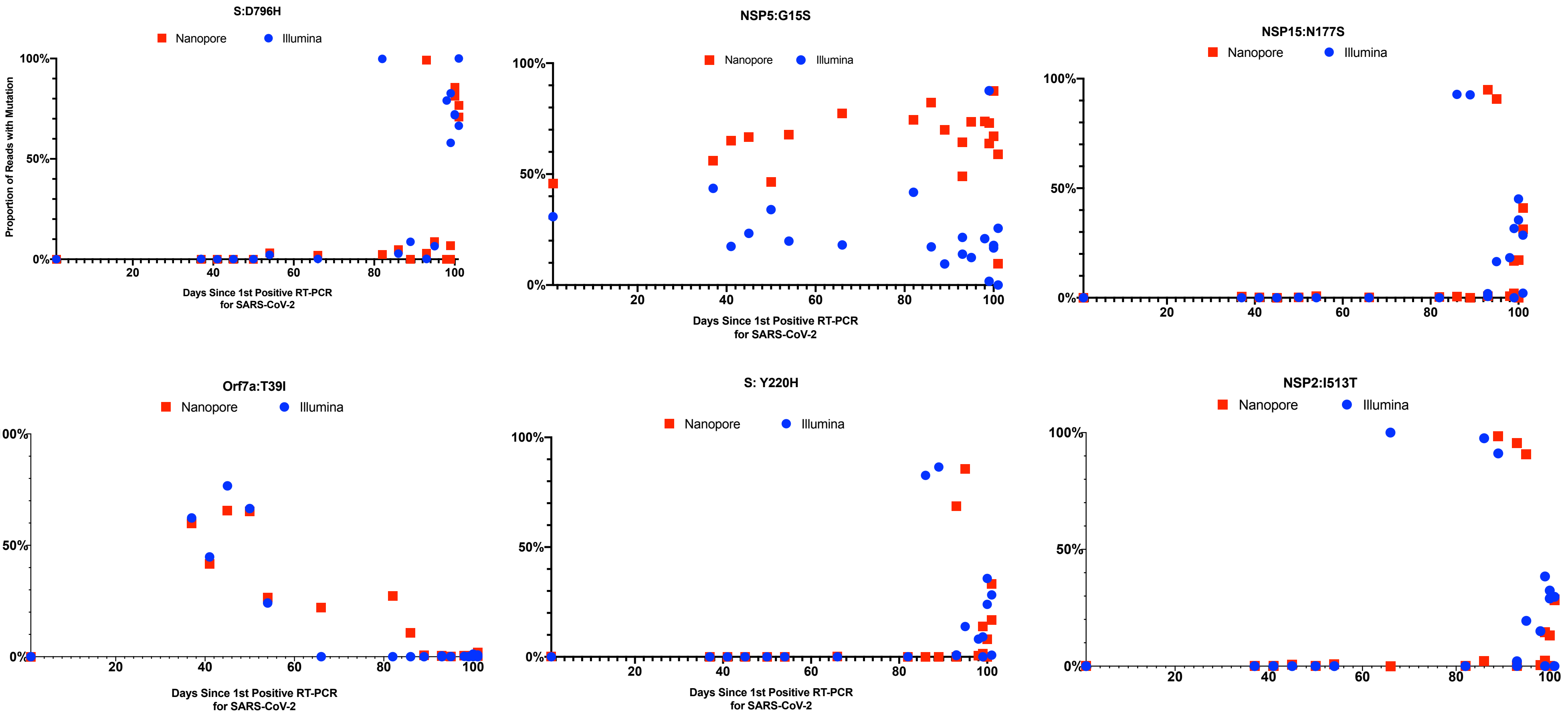




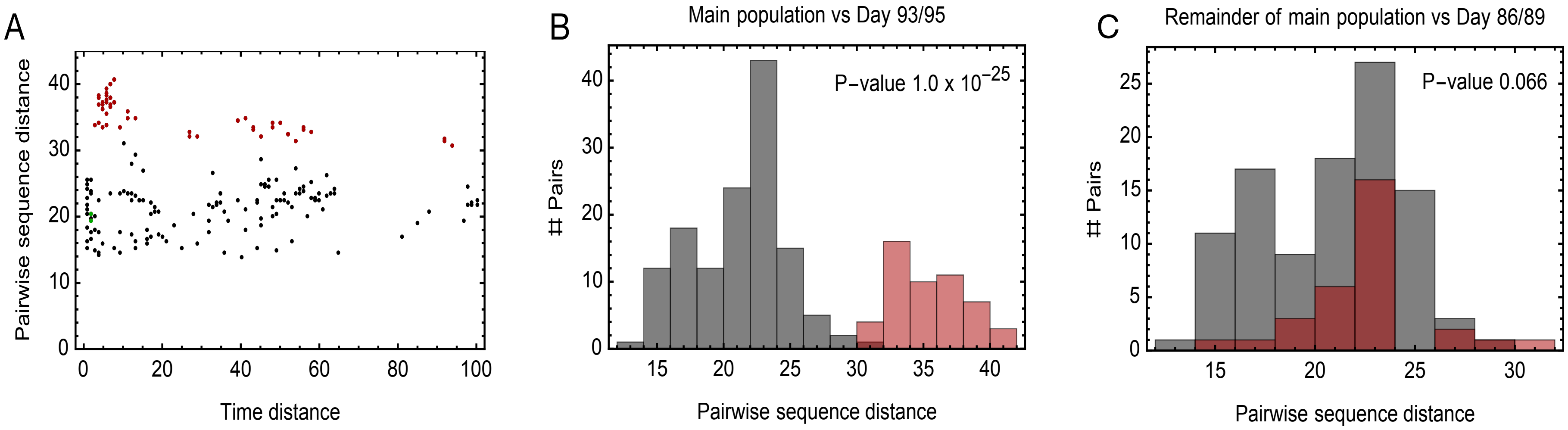
Supplementary Figure 3: Serial CT images following detection of SARS-CoV-2.
The patient initially presented with ground glass and peribroncho-vascular consolidation with associated intralobular septal thickening/reticulation and architectural distortion and interlobular septal thickening. By day 50 there is some improvement with evidence of resolving pnuemonitis, however, his condition deteriorated following the detection of bilateral pulmonary emboli, a well-recognized complication of SARS-CoV-2. Despite multiple therapeutic interventions, the patient’s condition deteriorated with worsening of inflammatory changes and chronic organizing pneumonia (COP), particularly on the left, and ongoing changes compatible with persistent SARS-CoV2 infection.

Supplementary Figure 4: SARS-CoV-2 antibody titres in convalescent plasma. Measurement of SARS-CoV-2 specific IgG antibody titres in three units of convalescent plasma (CP) by Euroimmun assay.

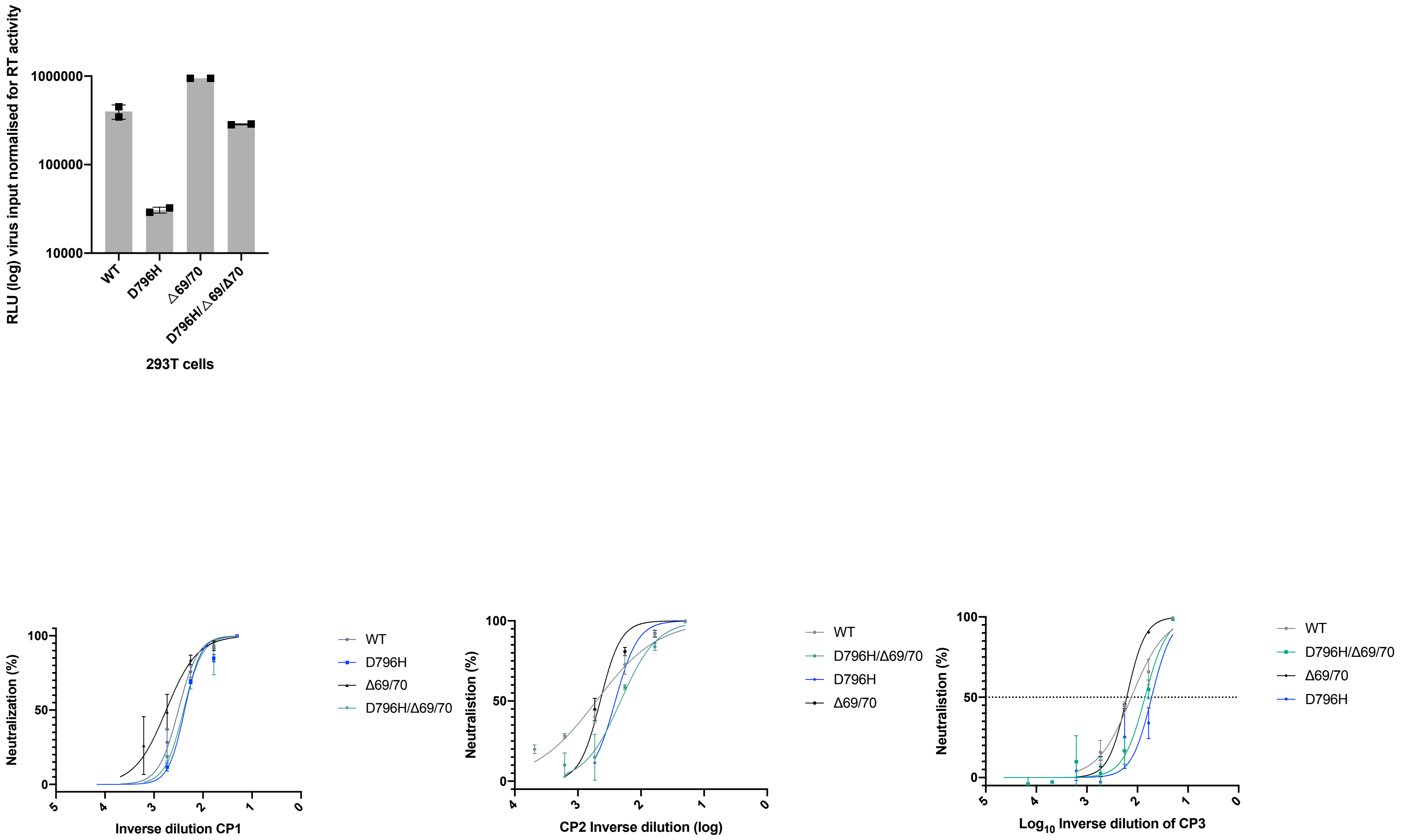




Supplementary Figure 5. Concordance between short-read (Illumina) and long-read single molecule (Oxford Nanopore) sequencing methods for twenty samples. Points are the frequency of the variant at each timepoint; only 20 samples were sequenced using the Illumina method. Boxes represent inter-quartile ranges. Error bars are 95% CI. There was good concordance for mutations between the two methods, and no significant difference between the proportion of reads measured by both methods.



Supplementary Figure 6: Additional evidence for within-host cladal structure. A. Pairwise distances between samples measured using the all-locus distance metric plotted against pairwise distances in time (measured in days) between samples being collected. Internal distances between samples in the proposed main clade are shown in black, distances between samples in the main clade and samples collected on days 93 and 95 are shown in red, and internal distances between samples collected on days 93 and 95 are shown in green. **B.** Pairwise distances between samples in the larger clade (black) and between these samples and those collected on days 93 and 95 (red). The median values of the distributions of these values are significantly different according to a Mann Whitney test. **C.** Pairwise distances between samples in the main clade, once those collected on days 86, 89, 93, 95 have been removed (black) and between these samples and those collected on days 86 and 89 (red). The median values of the distributions of these values are not significantly different at the 5% level according to a Mann Whitney test.



Supplementary Figure 7: In vitro infectivity and neutralisation sensitivity of Spike pseudotyped lentiviruses. Top: infection of target 293T cells expressing TMPRSS2 and ACE2 receptors using equal amounts of virus as determined by reverse transcriptase activity. Bottom: Representative Inverse dilution plots for Spike variants against convalescent plasma units 1-3. Data points represent mean % neutralisation and error bars represent standard error of the mean