Supplementary table 1. IgG neutralization data (0.2 mg/ml) for bCrN patients[a]

Sample	Time[b] (Months)	V1 191 (A) Tier 2[c]	NL4-3 (B) Tier 1A[c]	AC10 (B) Tier 2[c]	92BR025 (C) Tier 1B[c]	92UG024 (D) Tier 2[c]	CM244 (E) Tier 2[c]	VSV	# subtypes crossed
181-025	-36.9	43.6±9.1	21.9±6.2	74.8±8.6	36.8±4.2	37.5±8.9	33.6±2.6	169.9±13.9	5
181-027	-28.2	42.1±6.2	13.8±6.0	74.7±11.8	32.4±2.3	45.9±5.6	28.3±8.0	130.1±20.0	5
181-029	-20.4	27.1±5.0	13.7±9.5	66.6±4.3	25.9±3.8	38.9±2.4	24.9±4.3	147.8±43.5	5
181-031	-14.9	41.7±8.3	22.7±9.7	77.3±1.8	30.2±4.4	43.8±5.5	29.0±6.7	169.8±0.7	5
181-032	-11.0	34.2±3.9	22.3±10.1	73.2±10.8	33.9±0.9	38.9±5.5	36.9±3.8	138.6±23.4	5
181-034	-4.8	26.8±2.6	8.4±2.7	60.6±7.1	27.8±7.9	35.7±0.5	26.9±5.1	139.9±24.7	5
181-036	0.0	40.6±10.2	14.6±3.1	46.6±1.3	26.2±10.5	43.5±18.6	27.6±3.3	94.2±14.2	5
181-037	13.6	74.8±7.6	17.9±10.7	74.4±1.4	39.5±8.1	65.9±10.3	83.6±2.8	60.6±4.4	2
181-038	17.3	80.3±19.5	16.6±10.0	70.4±18.7	41.1±1.1	72.8±7.4	63.5±4.5	92.9±5.0	2
181-041	34.0	93.4±7.4	12.7±6.4	83.1±4.5	37.1±2.4	55.7±10.1	64.9±2.2	73.5±4.3	2
308-028	-71.4	20±2.8	0.4±0.6	0.0±0.2	7.3±1.9	39.3±9.4	61.3±9.3	89.2±6.8	4
308-029	-61.3	13.1±3.7	0.0±0.3	0.0±0.1	5.7±2.0	16.5±2.5	50.9±3.7	66.2±4.0	4
308-030	-55.5	8.2±0.4	2.0±2.4	0.0±0.2	1.1±1.2	7.8±1.7	26.6±1.4	87.2±8.4	5
308-031	-49.1	17.5±1.4	1.7±1.2	9.1±4.4	9.1±2.2	20.8±3.6	33.0±6.2	85.7±4.5	5
308-033	-43.1	12.3±0.8	0.0±0.3	6.8±1.8	2.5±2.6	10.5±5.0	40.8±3.4	62.5±4.1	5
308-034	-39.5	20.6±3.1	0.9±2.6	10.6±3.0	4.9±2.8	20.0±5.1	45.2±3.5	64.5±4.3	5
308-036	-31.9	12.6±2.6	0.6±1.3	13.0±3.2	5.2±1.3	17.3±9.9	32.3±2.3	72.2±7.0	5
308-038	-22.3	23.3±5.8	0.5±1.0	9.3±1.2	9.2±3.6	23.2±5.7	40.9±4.7	71.8±4.6	5
308-040	-14.0	23.2±2.5	1.2±0.8	11.0±1.1	19.3±6.4	25.7±3.7	33.2±3.9	77.3±7.2	5
308-041	0.0	16.4±5.6	2.2±1.1	25.0±6.8	15.5±4.3	13.4±19.3	17.4±3.0	73.1±10.0	5
308-043	8.5	42.1±2.9	5.0±5.5	41.7±4.9	29.8±9.6	29.7±3.1	52.7±1.9	87.8±2.8	4
308-044	20.2	51.4±3.7	0.1±0.8	55.8±11.7	30.4±3.0	42.0±14.9	71.7±3.5	82.8±11.2	3
363-008	-45.6	87.7±5.3	6.4±6.3	42.6±14.9	41.6±9.5	27.9±3.1	32.1±1.2	117.9±43.1	4
363-009	-39.0	95.8±4.3	16.7±14.5	56.9±3.2	56.2±9.5	50.1±11.0	54.2±4.3	98.5±22.3	1
363-010	-33.5	100.0±13.7	4.3±5.4	61.6±6.0	85.2±22.1	120.6±23.9	80.3±4.3	117.8±18.2	1
363-011	-16.9	61.5±3.7	2.1±2.7	56.2±9.2	31.6±7.9	43.5±8.8	39.3±2.0	105.4±21.3	4
363-012	-10.5	54.3±9.1	3.8±1.7	55.1±5.1	36.3±3.2	47.6±8.4	46.9±4.7	83.7±4.6	4
363-013	-6.4	71.5±1.8	3.0±0.8	58.9±8.4	41.4±11.7	72.3±16.3	58.7±6.0	111.3±17.4	2
363-014	0.0	26.7±14.4	2.4±0.3	15.9±3.7	14.8±0.4	35.5±18.4	24.4±2.5	50.5±3.3	5
363-015	12.2	60.2±5.7	7.8±4.3	56.6±4.1	43.2±4.5	53.6±11.2	27.2±6.2	97.8±6.8	3
363-016	17.7	52.6±9.4	1.8±1.1	54.6±14.4	31.0±0.8	52.2±13.9	27.1±3.5	72.1±3.7	3
363-017	21.8	46.1±7.7	2.1±2.3	56.9±5.3	32.9±1.2	62.2±13.3	28.9±4.0	67.2±2.4	4
488-003	-56.9	39.7±6.4	2.6±1.5	88.4±2.4	19.3±4.5	52.3±5.3	74.0±4.4	89.6±20.7	3
488-004	-50.0	48.3±13.0	3.6±1.2	92.4±8.5	24.8±9.2	74.6±13.3	87.2±4.4	81.3±4.7	3
488-005	-44.9	32.7±3.4	0.8±1.3	66.7±4.7	24.6±2.8	58.4±11.2	89.1±2.7	82.5±0.5	3
488-006	-38.7	42.5±2.9	1.7±1.8	92.0±9.0	18.7±1.6	55.6±7.5	85.0±4.9	82.5±7.2	3
488-007	-33.5	43.0±2.5	6.2±5.0	90.5±11.7	18.5±3.6	67.6±12.4	71.3±4.6	102.4±10.7	3
488-009	-25.9	49.2±1.9	4.7±4.3	84.9±12.9	23.4±2.6	60.3±8.5	74.6±3.2	120.1±5.1	3
488-011	-19.2	59.9±2.7	7.5±6.0	56.1±15.3	33.8±4.6	72.5±9.4	85.5±7.9	84.8±5.8	2
488-012	-14.0	86.8±6.6	5.5±3.7	64.0±0.8	76.2±9.3	93.0±3.9	66.6±11.1	91.9±6.0	1
488-013	0.0	16.9±1.9	1.2±0.8	48.7±9.9	13.9±2.3	36.7±18.1	46.9±2.6	77.9±4.4	5
488-015	7.4	41.0±2.0	2.9±2.3	74.9±1.6	18.7±1.4	50.6±1.4	49.6±2.2	79.7±3.3	4
488-016	16.6	50.0±9.3	1.9±2.4	83.0±7.0	25.1±1.8	56.8±11.9	57.5±5.1	83.3±3.5	2
488-017	21.4	67.8±2.9	5.4±3.7	88.8±7.1	28.5±3.3	59.2±10.9	63.5±2.7	88.6±0.7	2
528-001	-52.1	60.4±2.8	0.8±4.0	86.8±7.2	41.5±5.4	27.2±3.8	50.4±5.1	118.4±37.0	3
528-002	-44.7	93.9±8.1	0.0±0.6	58.5±2.4	37.9±6.0	71.7±9.5	74.4±10.0	119.8±8.4	2
528-003	-37.1	104.4±2.4	0.0±0.2	36.6±3.3	46.6±10.8	53.1±16.5	17.9±1.7	114.2±21.1	3
528-005	-31.2	102.7±5.9	0.0±0.2	27.6±3.7	23.9±11.0	44.1±13.2	11.8±4.9	116.8±5.4	4
528-006	-25.0	26.3±10.3	0.0±1.4	12.0±6.1	1.9±2.2	36.5±14.6	13.9±1.2	118.3±4.8	5
528-008	-16.3	58.0±2.9	0.0±0.1	23.1±2.9	11.0±3.9	29.6±10.8	16.6±1.0	128.9±24.5	4
528-009	-11.7	75.6±15.0	0.0±0.5	15.8±1.8	3.3±2.0	46.7±8.0	11.9±2.1	133.5±4.0	4
528-010	0.0	49.1±11.3	1.7±0.9	13.4±2.7	6.8±3.0	7.1±5.3	13.8±1.1	67.1±2.2	5
528-012	8.8	79.9±10.3	0.0±0.1	4.3±3.2	0.7±0.6	13.8±3.3	3.4±2.5	134.2±12.0	4
528-013	13.5	99.3±5.8	0.0±0.5	14.6±3.4	0.0±1.7	11.1±8.4	7.5±5.1	133.8±11.3	4
528-014	18.9	108.3±17.8	5.5±6.4	19.6±2.2	1.3±1.4	15.4±7.4	11.7±0.4	155.1±12.1	4
528-015	31.1	35.2±7.3	0.0±2.2	45.2±12.2	7.4±2.6	22.8±7.1	15.9±7.0	85.0±9.1	5
541-001	-50.7	80.2±12.5	0.4±3.9	42.2±2.6	45.0±17.8	64.7±21.8	52.7±5.3	119.9±1,7	2
541-002	-41.7	107.9±11.4	0.0±0.8	48.9±4.6	52.7±6.6	76.7±8.5	66.1±4.0	139.2±14.9	1
541-003	-38.1	78.0±7.7	0.0±0.5	25.4±3.7	26.9±14.2	88.5±29.7	58.8±7.5	123.1±10.1	2
541-005	-31.6	70.9±2.1	0.0±1.7	20.0±2.2	17.4±8.4	58.5±40.5	61.5±8.1	140.5±7.3	2
541-007	-24.7	45.4±3.6	0.0±0.7	19.1±4.1	9.7±4.5	81.9±9.8	51.6±3.7	131.9±16.8	3
541-009	-17.4	56.9±3.9	0.0±1.6	24.6±7.2	13.3±2.0	72.5±24.7	44.4±13.2	131.5±14.7	3
541-011	0.0	34.9±4.0	4.5±0.5	40.6±6.0	26.3±1.8	46.4±2.7	48.5±2.7	62.6±4.8	5
541-012	4.4	99.6±6.0	2.5±4.4	53.0±5.7	35.4±8.6	124.3±28.1	70.2±6.9	102.2±9.9	2
541-013	20.2	122.8±17.8	0.3±3.8	65.5±20.0	42.8±16.0	75.6±6.4	71.2±5.7	117.0±7.7	2

[a] Numbers indicate percent luciferase activity (counts per second ± standard deviation). White indicates > 50% luciferase activity; yellow indicates <50% luciferase activity but >30%; orange indicates <30% luciferase activity but >10%; red indicates <10% luciferase activity.

[b] Time is indicated as months. Time 0 corresponds to the last time point included in the previous study.

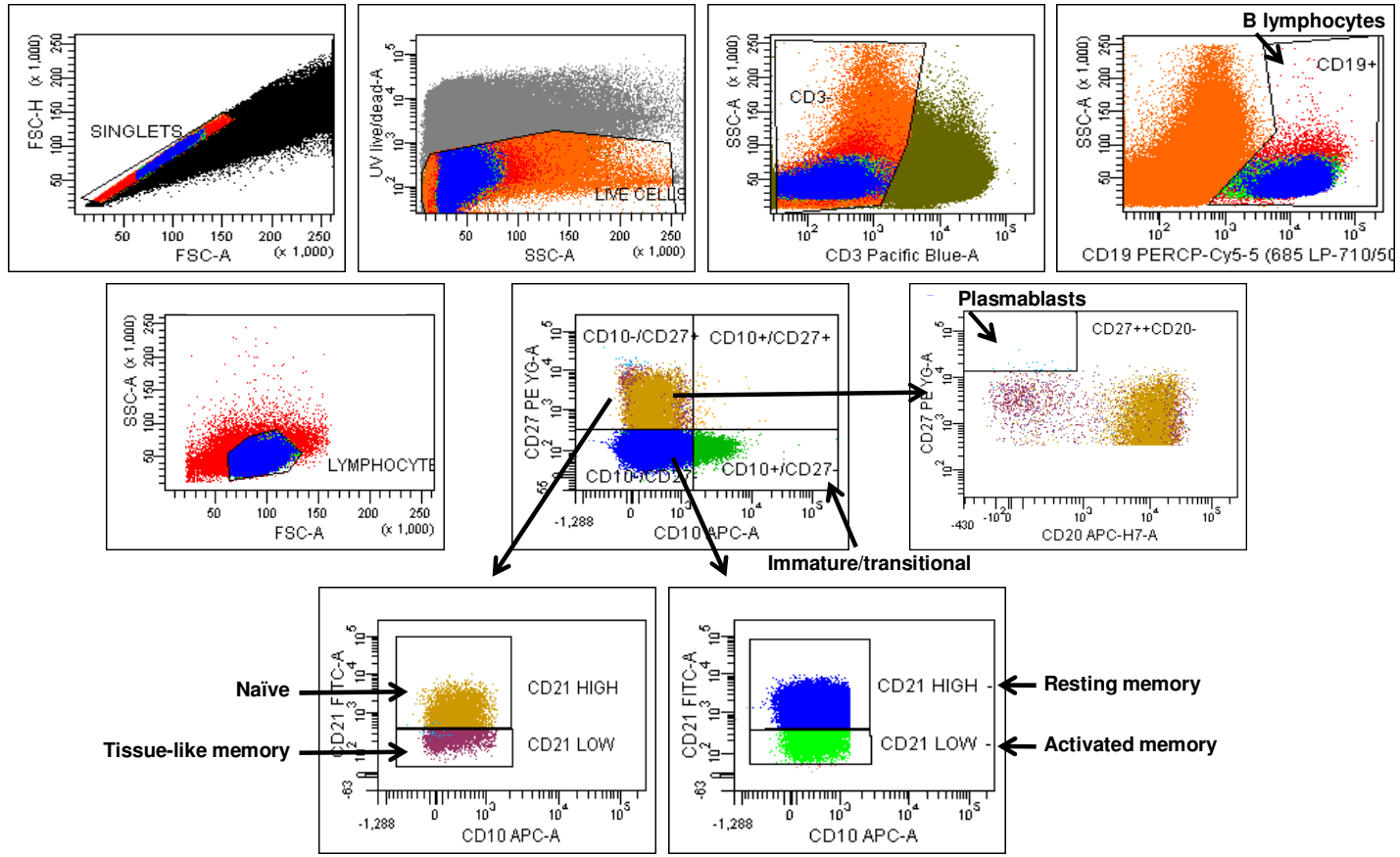
[c] Clades and Tier classifications are indicated.

Supplementary table 2. IgG neutralization data (0.2 mg/ml) for control patients[a]

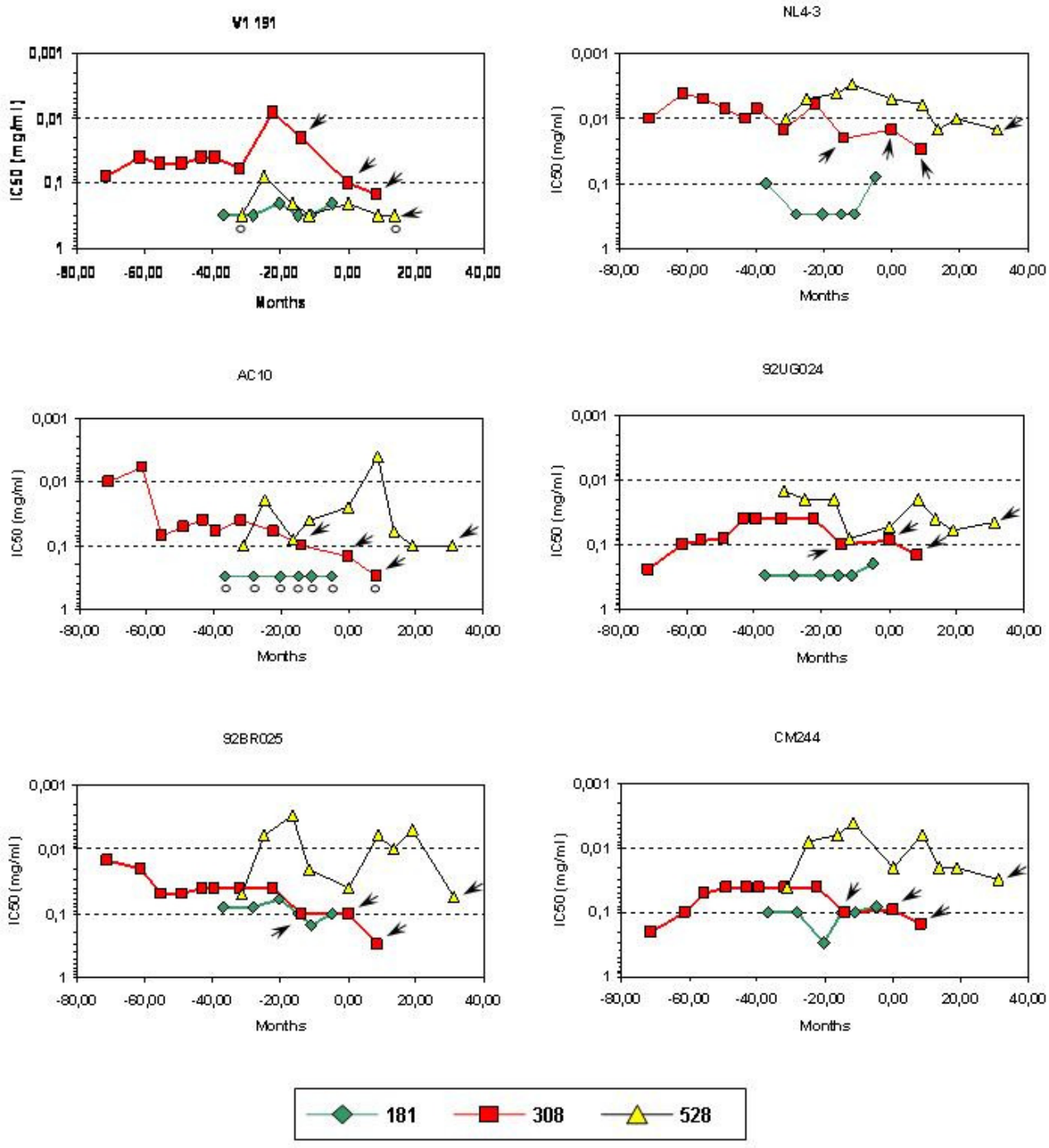
Sample	Time[b] (Months)	V1 191 (A) Tier 2[c]	NL4-3 (B) Tier 1A[c]	AC10 (B) Tier 2[c]	92BR025 (C) Tier 1B[c]	92UG024 (D) Tier 2[c]	CM244 (E) Tier 2[c]	VSV	# subtypes crossed
108-009	-36.7	51.4±25.6	5.1±1.2	77.8±5.7	35.3±1.7	69.0±3.4	93.2±15.0	120.7±1.2	2
108-010	-32.1	42.3±30.4	2.7±2.6	57.2±16.3	30.9±4.0	66.7±12.3	99.7±4.7	112.5±8.6	3
108-011	-27.3	60.4±29.5	9.8±3.7	62.9±10.3	32.6±1.7	50.2±12.5	107.5±2.7	141.1±6.3	2
108-012	-14.4	42.8±14.9	7.3±3.6	54.0±10.3	32.9±2.6	80.1±4.6	101.0±6.5	119.5±11.2	3
108-014	-12.4	54.3±21.5	5.0±2.5	57.7±9.8	38.3±2.3	85.6±5.9	107.1±13.4	147.1±3.9	2
108-016	-5.3	49.3±19.4	7.8±5.3	49.5±12.7	27.3±1.6	84.3±5.7	122.8±21.6	155.1±12.2	3
108-018	0.0	53.7±15.4	11.5±8.9	55.3±21.1	36.2±3.8	70.7±1.8	95.7±7.8	126.1±5.8	2
108-019	5.5	48.7±13.4	5.6±2.0	39.4±28.6	44.4±7.0	60.4±7.8	66.3±0.9	145.9±10.2	3
108-021	22.7	47.9±2.1	4.1±3.1	73.2±2.2	48.0±6.0	70.4±3.8	87.2±7.3	106.0±9.9	3
108-022	27.3	49.2±3.8	22.8±11.5	70.9±4.5	49.1±6.0	79.1±7.8	100.6±0.8	110.7±7.3	3
279-008	-54.8	11.0±2.9	7.7±9.8	60.2±3.2	22.1±1.5	105.8±9.6	146.2±18.9	163.0±0.94	3
279-009	-50.0	29.8±10.8	1.0±0.9	40.2±1.9	34.6±4.0	81.7±0.6	116.5±10.5	123.9±5.7	3
279-012	-30.7	31.5±10.2	0.6±1.3	29.1±1.9	22.6±1.8	56.5±10.5	105.9±8.4	124.0±5.1	3
279-014	-21.3	16.0±1.8	6.7±6.4	38.2±5.4	8.9±1.1	79.8±2.4	108.3±8.4	163.5±2.4	3
279-015	-17.0	18.0±10.6	1.0±2.5	43.6±3.6	5.3±0.9	74.2±4.6	91.0±7.9	152.6±1.7	3
279-016	-11.7	46.2±17.6	3.8±5.3	43.6±2.9	27.1±3.0	76.9±16.7	96.9±11.6	114.4±8.4	3
279-018	0.0	19.9±6.5	2.5±2.6	43.7±2.9	39.7±4.9	92.7±20.2	90.4±35.1	112.3±2.6	3
279-019	6.4	11.8±1.2	5.4±6.3	54.6±6.7	40.6±34.6	96.1±11.3	97.6±7.8	145.7±5.7	3
279-022	18.4	0.0±1.1	0.0±0.3	89.2±4.7	27.7±8.7	87.9±21.7	121.0±19.5	112.7±13.4	3
279-025	28.9	76.9±23.4	17.4±12.7	88.7±4.7	51.1±9.4	64.6±13.3	107.4±1.9	119.1±6.6	1
296-023	-42.2	39.5±9.3	11.4±14.0	97.5±17.1	58.4±10.0	81.0±8.5	47.0±1.0	63.6±0.7	3
296-026	-38.1	25.4±19.5	1.8±2.9	85.2±12.9	88.7±14	110.7±8.2	70.1±6.3	100.9±10.5	2
296-028	-31.2	33.3±12.8	1.4±1.3	72.8±8.2	50.1±6.6	68.2±7.1	37.9±2.9	81.5±6.2	3
296-029	-26.6	30.1±6.2	5.8±6.7	70.2±6.4	79.7±8.8	96.2±23.6	72.3±6.6	67.8±8.5	2
296-031	-19.0	32.4±7.6	25.1±12.7	63.8±13.1	92.7±22.8	98.9±2.1	67.6±0.3	87.4±6.3	2
296-033	-13.8	32.7±6.3	17.6±6.7	92.5±19.8	96.6±16.1	102.9±3.2	70.3±4.4	95.3±16.5	2
296-035	-6.2	20.2±14.9	7.4±9.6	109.0±2.2	74.4±13.3	77.9±4.1	63.3±3.9	91.9±24.6	2
296-037	0.0	55.1±21.0	13.9±14.8	106.3±3.7	58.8±4.1	86.0±10.8	74.1±6.1	132.1±13.5	1
296-039	6.7	36.5±6.2	17.1±13.9	89.1±28.4	69.5±3.8	72.1±16.1	59.5±7.0	100.6±6.4	2
296-040	9.0	29.9±5.1	18.1±7.8	87.2±12.1	40.6±9.6	62.9±5.8	39.5±5.2	83.9±12.1	4
296-041	12.6	36.0±14.5	15.5±7.5	98.2±16.6	69.8±5.9	91.1±16.3	61.9±10.9	92.6±23.3	2
296-042	17.9	28.7±9.9	14.7±18.4	91.6±9.6	78.1±7.4	99.7±12.1	59.9±1.2	107.8±14.6	2
326-002	-53.7	54.5±4.0	17.0±10.0	104.0±10.3	89.5±10.1	81.4±5.8	97.9±14.1	112.8±8.9	1
326-004	-44.5	37.1±3.5	4.7±2.1	109.3±7.1	42.3±12.3	68.0±20.7	92.2±24.2	107.0±10.6	3
326-006	-37.4	46.0±4.2	1.6±0.4	108.9±19.6	35.6±0.6	61.8±8.3	117.8±3.4	98.2±15.5	3
326-009	-30.10	53.5±7.5	25.1±6.5	109.3±19.3	46.0±9.8	77.0±17.8	93.2±10.3	104.0±21.8	2
326-011	-22.5	58.5±8.2	11.3±6.8	116.9±9.2	35.6±10.7	69.8±4.9	92.8±12.2	121.3±8.7	2
326-013	-14.2	54.3±12.7	8.1±7.8	92.2±8.4	38.5±0.8	71.4±3.0	67.3±0.9	117.7±13.2	2
326-023	-8.7	37.5±7.1	2.4±2.9	100.9±4.2	17.3±5.6	56.1±3.4	66.8±9.9	121.1±1.6	3
326-026	0.0	64.5±12.7	15.6±5.4	81.4±13.6	39.4±9.5	60.9±1.5	61.5±2.7	134.9±4.4	2
326-028	6.2	73.0±13.1	9.6±8.7	76.4±15.4	55.1±1.1	56.8±4.4	57.7±5.8	129.2±9.4	1
326-030	23.4	62.1±8.9	3.5±4.6	70.9±14.3	50.7±6.3	58.8±2.0	58.4±4.9	132.3±9.8	1
405-006	-47.5	51.7±8.8	6.1±7.3	85.2±8.3	33.8±1.3	75.2±5.2	96.6±7.2	122.1±7.1	2
405-007	-37.4	49.2±1.9	8.6±4.5	86.3±6.0	37.9±1.2	72.6±7.5	88.4±14.5	114.7±7.2	3
405-008	-28.2	59.4±4.7	7.1±6.1	95.9±2.1	25.6±5.4	80.6±17.3	101.8±12.1	127.5±4.8	2
405-009	-22.0	55.5±3.5	3.1±1.8	91.2±19.8	37.3±4.4	54.5±16.5	93.3±12.0	126.6±2.7	2
405-010	-17.4	50.6±9.6	1.9±2.8	91.7±6.5	33.9±0.3	59.4±5.4	96.2±14.6	128.0±1.1	2
405-011	-12.4	51.4±8.3	0.0±0.5	80.2±12.0	32.2±6.6	60.4±1.4	81.7±13.4	127.6±8.1	2
405-013	0.0	61.5±14.9	7.8±10.6	70.7±16.0	44.8±3.3	74.8±3.5	75.6±7.1	124.2±4.9	2
405-014	10.3	16.2±2.1	2.9±0.6	77.2±19.9	8.5±1.3	58.8±5.7	84.5±20.9	133.3±4.8	3
405-016	17.7	15.9±3.6	2.9±1.1	99.6±10.0	8.6±1.6	77.5±4.5	107.3±3.0	142.2±4.0	3
405-017	20.9	74.2±3.3	8.8±2.6	88.6±2.1	52.0±2.6	67.7±2.9	77.7±11.4	124.3±2.8	1
423-005	-55.3	140.9±6.9	3.8±3.8	104.9±4.7	77.2±5.1	64.3±9.3	76.5±7.4	87.34±5.1	1
423-007	-46.3	140.3±9.5	7.2±2.8	92.3±8.2	62.23±3.5	63.1±16.8	73.3±1.7	78.9±1.7	1
423-009	-37.2	102.7±10.8	0.8±1.6	81.7±8.3	61.7±6.9	56.7±13.9	77.1±3.9	91.8±0.9	1
423-011	-30.7	110.8±11.6	0.0±1.4	89.4±0.9	63.4±18.1	55.8±13.4	69.2±1.7	90.0±3.7	1
423-012	-25.2	86.5±11.4	0.0±0.9	102.0±9.4	65.5±6.1	57.7±20.1	78.4±10.6	109.3±4.2	1
423-013	-17.6	91.5±3.9	2.2±4.1	97.5±6.1	57.6±6.7	63.2±12.1	66.7±8.5	90.1±5.7	1
423-015	-14.0	94.5±6.2	2.9±2.7	97.1±9.7	58.0±8.2	63.1±21.4	77.0±1.0	99.3±6.0	1
423-016	-6.6	98.3±6.0	7.9±7.8	85.7±6.8	59.8±4.3	59.5±3.7	58.3±0.7	87.2±6.1	1
423-017	0.0	116.8±1.5	3.0±1.5	98.3±6.9	71.5±13.1	70.3±9.2	99.2±14.7	121.1±2.6	1
423-018	18.8	72.1±7.8	4.3±6.4	80.9±2.2	41.3±7.3	50.7±5.8	59.0±4.9	93.0±1.2	2

[a] Numbers indicate percent luciferase activity (counts per second ± standard deviation). White indicates > 50% luciferase activity; yellow indicates <50% luciferase activity but >30%; orange indicates <30% luciferase activity but >10%; red indicates <10% luciferase activity.
[b] Time is indicated as months. Time 0 corresponds to the last time point included in the previous study.
[c] Clades and Tier classifications are indicated.

Supplementary Figure 1



Supplementary Figure 1 . Flow-cytometric gating strategy for B-cell subpopulation analysis. Representative flow cytometry gating strategy for sample 308-040 (bCrN patient with broadly cross-reactive neutralizing activity at this time point). B lymphocytes (CD3- CD19+) were gated into four subsets according to their expression of CD10 and CD27 (CD10- CD27+, CD10+ CD27+, CD10- CD27- and CD10+ CD27-). Within these subsets, six B cell subpopulations were further defined as immature/transitional (CD10+ CD27-), naïve (CD10- CD27- CD21hi), tissue-like memory (CD10- CD27- CD21lo), resting memory (CD10- CD27+ CD21hi), activated memory (CD10- CD27+ CD21lo) and plasmablasts (CD10- CD27++ CD20- CD21lo).



Supplementary Figure 2. Evolution of IgG neutralization titers during the periods of broad cross-reactive neutralizing responses in patients 181, 308 and 528 (IC50s). Values indicate the concentration of purified IgG that reduces the infectivity by 50% (IC50) and are indicated by a green dimond and green solid line, patient 181; red square and red solid line, patient 308 and yellow triangle and black solid line, patient 528. Open circles indicate that 50% infectivity reduction was reached at the highest IgG concentration tested (0.3mg/ml). The IC50s corresponding to times in which the patient was on cART are by arrows. Time is indicated as months (x axes). Time 0 corresponds to the last time point included in the previous study(15).