# Pharmacokinetics of High-titer Anti-SARS-CoV-2 Human Convalescent Plasma in High-risk Children

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**Supplemental Table 1. Study participants (recipients).**

| # | Sex | Age | Race / Ethnicity | Co-morbidities | Weight (kg) | Height / length (cm) | Time to plasma [1] (days) | Recipient / Donor Blood type | Plasma dose (mL/kg) |
|---|---|---|---|---|---|---|---|---|---|
| **1** | M | 9y | Hispanic | DICER1-associated parietal lobe sarcoma | 44.6 | 141 | 5 | O+/O+ | 5 |
| **2** | F | 3m | AA | Prematurity, acyanotic Tetralogy of Fallot, chronic lung disease, planned for corrective heart surgery | 4.5 | 53 | 3 | B+/B+ | 5 |
| **3** | F | 4y | Asian | Immunodeficiency associated with CARD 11 mutation, IVIG[2] dependent | 13.8 | 98 | 5 | O+/O+ | 5 |
| **4** | M | 16y | White | Crohn's disease, receiving infliximab | 64.3 | 172.9 | 4 | A-/A- | 4 |
| **5** | M | 16y | AA | Asthma | 65.8 | 174 | 4 | O+/O+ | 4 |
| **6** | F | 15y | White | Chromosome 18q deletion, CVID, IVIG[2] dependent, chronic lung disease | 25.4 | 135.9 | 5 | O+/O+ | 5 |
| **7** | F | 5y | White | SMA type 1 | 12.5 | 88 | 5 | O+/O+ | 5 |
| **8** | M | 17y | White | S/P Wilms tumor and BMT, asthma | 49.1 | 162.5 | 5 | A+/A+ | 4 |
| **9** | F | 6y | White | Prematurity, chronic lung disease, CVID, IVIG[2] dependent | 16.4 | 106.9 | 3 | O+/O+ | 5 |
| **10** | F | 5y | White | Ataxia telangiectasia, IVIG[2] dependent | 19.1 | 102 | 7 | O+/O+ | 5 |
| **11** | M | 13y | White | Cerebral palsy, epilepsy, pulmonary insufficiency | 41.7 | 144.8 | 3 | A+/A- | 5 |
| **12** | M | 6y | AA | Caroli syndrome, ARPKD, liver and kidney transplant, tracheostomy | 14.1 | 90 | 2 | A+/A+ | 5 |
| **13** | M | 9y | White | Ataxia Telangiectasia, chronic lung disease | 31.5 | - | 5 | O+/O+ | 5 |

[1]Time from symptom onset / exposure to administration of COVID-19 convalescent plasma. [2]P#3 - received IVIG, 10 days before convalescent plasma and then every 3 weeks; P#6 - received SubQ-IG, 4 days before convalescent plasma and then every 7 days; P#9 - received SubQ-IG, 4 days before convalescent plasma and then every 7 days; P#10 - received SubQ-IG, 5 days before convalescent plasma and then every 7 days. F - Female; M - male; y - years; m - months; AA - African American; ARPKD - autosomal recessive polycystic kidney disease; BMT - bone marrow transplant; CVID - common variable immune deficiency; IVIG - intravenous immunoglobulin; SMA - spinal muscular atrophy.

**Supplemental Table 2. Clinical presentation at study entry.**

| Recipient # | Infected children[1] | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **SARS-CoV-2 NP RT-PCR** | 8 (100%) | Pos | Pos[2] | Neg | Neg | Neg | Pos | Pos | Neg | Neg | Pos | Pos | Pos | Pos |
| **Fever** | 8 (100%) | Y | Y | N | N | N | Y | Y | N | N | Y | Y | N | Y |
| **Duration of fever (days)** | 3 days | 3 | 3 | NA | NA | NA | 5 | 5 | NA | NA | 1 | 1 | NA | 2 |
| **Cough** | 6 (75%) | Y | N | N | N | Y | Y | Y | N | N | Y | Y | N | Y |
| **Shortness of breath** | 4 (50%) | N | Y | N | N | Y | Y | Y | N | N | N | Y | N | N |
| **Congestion and/or runny nose** | 3 (37.5%) | Y | N | N | N | Y | Y | N | N | N | Y | Y | Y | Y |
| **Sore throat** | 1 (12.5%) | N | NA | N | N | Y | NA | N | N | N | Y | NA | N | N |
| **Diarrhea** | 1 (12.5%) | N | N | N | N | N | N | N | N | N | Y | N | N | N |
| **Vomiting** | 1 (12.5%) | N | N | N | N | N | N | Y | N | N | N | N | N | N |
| **Headache** | 1 (12.5%) | N | NA | N | N | Y | NA | N | N | N | N | NA | N | Y |
| **Rash** | 0 (0%) | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Muscle aches** | 2 (25%) | Y | NA | N | N | N | NA | N | N | N | N | NA | N | Y |
| **Loss of smell or taste** | 0 (0%) | N | NA | N | N | N | NA | N | N | N | N | NA | N | N |
| **Hospitalization** | 5 (62.5%) | Y | Y | N | N | N | Y | Y | N | N | N | Y | N | N |
| **Length of admission (days)** | 7 days | 3 | 14 | NA | NA | NA | 4 | 7 | NA | NA | NA | 23 | NA | NA |
| **Admission to PICU** | 4 (50%) | N | Y | N | N | N | Y | Y | N | N | N | Y | N | N |
| **Length of admission to PICU (days)** | 5 days | NA | 4 | NA | NA | NA | 4 | 6 | NA | NA | NA | 6 | NA | NA |
| **Need for supplemental oxygen** | 4 (50%) | N | Y | N | N | N | Y | Y | N | N | N | Y | N | N |
| **Need for non-invasive positive pressure ventilation** | 3 (37.5%) | N | N | N | N | N | Y | Y | N | N | N | Y | N | N |
| **Other therapy for COVID-19** | 3 (37.5%) | N | N | N | N | N | Y[3] | Y[3] | N | N | N | Y[3] | N | N |

[1]Children with positive SARS-CoV-2 PCR; Testing performed using research and/or clinically approved tests; [2]Positive by clinically approved test only. N (%) or median days are presented. [3]Remdesivir and dexamethasone. PICU – Pediatric Intensive Care Unit; NA - non-applicable.

**Supplemental Table 3. Laboratory studies at presentation.**

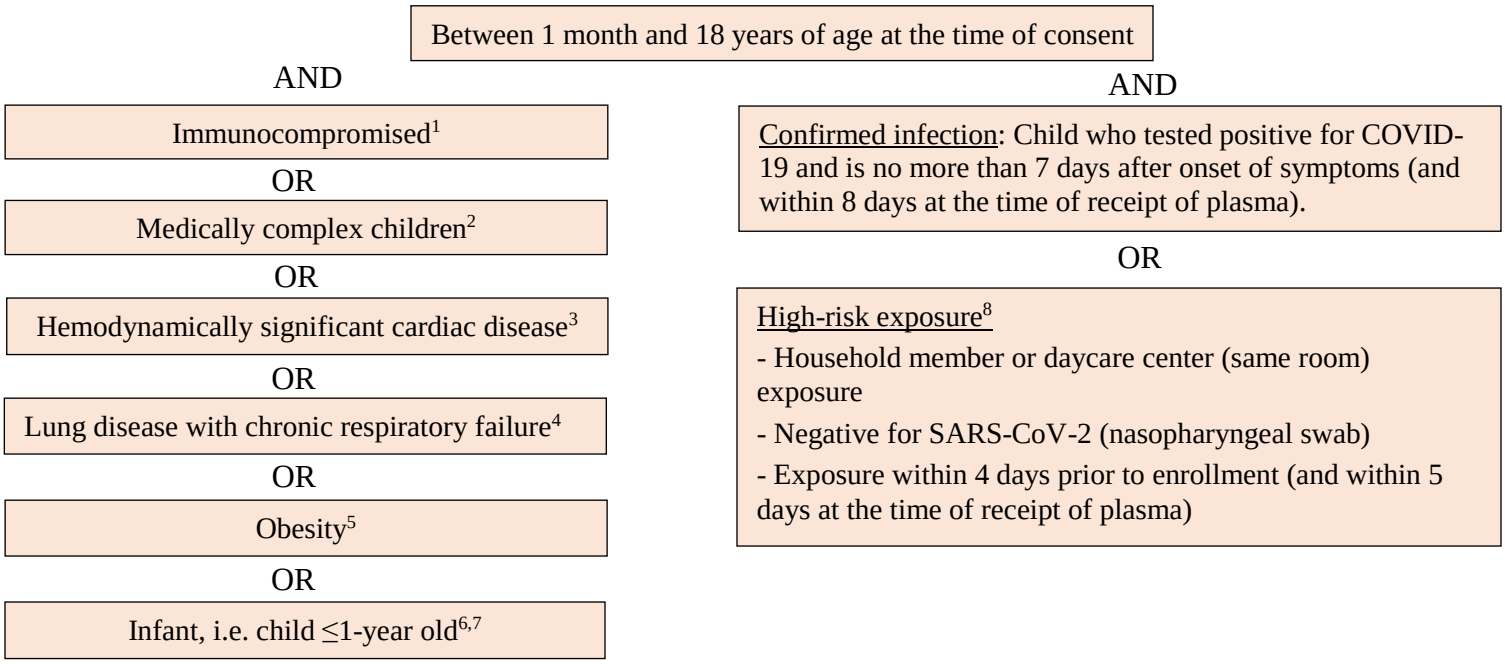
| Recipient # | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **WBC (k/mm^3)** | 2 | 12.41 | 28 | 5.28 | 4.78 | 18.78 | 13.08 | 6.82 | 5.12 | 3.74 | 8.18 | 8.78 | 4.69 |
| **HGB (g/dL)** | 6.6 | 15.2 | 10 | 14.2 | 15 | 14.6 | 13 | 14.6 | 10.5 | 13.1 | 15.2 | 12.8 | 14.4 |
| **Platelets (k/mm^3)** | 46 | 321 | 184 | 208 | 309 | 264 | 361 | 288 | 251 | 225 | 166 | 526 | 292 |
| **Neutrophil Count (k/mm^3)** | 1.82 | 4.59 | 2.25 | 2.65 | 2.1 | 18.02 | 8.41 | 3.6 | 1.05 | 2.22 | 6.88 | 4.32 | 2.23 |
| **Lymphocyte Count (k/mm^3)** | 0.04 | 6.58 | 25.59 | 1.94 | 1.79 | 0.25 | 3.94 | 2.17 | 3.59 | 1.04 | 0.71 | 3.75 | 1.51 |
| **Sodium (mEq/L)** | 136 | 137 | 138 | 139 | 141 | 134 | 133 | 140 | 140 | 140 | 146 | 137 | 141 |
| **BUN (mg/dL)** | 11 | 10 | 10 | 14 | 16 | 6 | 3 | 17 | 14 | 12 | 9 | 8 | 7 |
| **Serum Creatinine (mg/dL)** | 0.5 | 0.2 | 0.2 | 0.6 | 0.9 | 0.3 | 0.2 | 1.1 | 0.3 | 0.3 | 0.4 | 0.3 | 0.3 |
| **ALT (U/L)** | 35 | 14 | 13 | 18 | 17 | 27 | 18 | 21 | 13 | 31 | 13 | 19 | 51 |
| **CRP (mg/dL)** | NA | <0.1 | NA | NA | NA | 9.1 | 1.2 | NA | NA | NA | 5.3 | NA | NA |

ALT – alanine aminotransferase test; BUN – blood urea nitrogen; CRP – c-reactive protein; HGB – hemoglobin; NA – non-applicable; WBC – white blood cell count.

**Supplemental Table 4. Follow up evaluation 7 to 60 days post-transfusion of convalescent plasma.**

| Recipient # | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fever** | N | N | N | Day 10-12 | N | N | N | N | N | N | N | N | N |
| **Cough** | Until day 9 | N | N | Day 10-12 | N | N | N | N | N | Until day 10 | Y | N | N |
| **Shortness of breath** | N | N | N | N | N | Resolved at day7 | N | N | N | N | Y | N | N |
| **Congestion and/or runny nose** | N | N | N | N | N | N | N | N | N | Y | Y | Y | N |
| **Sore throat** | N | N | N | Day 10-12 | N | NA | N | N | N | N | NA | N | N |
| **Diarrhea** | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Vomiting** | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Headache** | Days 7-11 | NA | N | N | N | NA | N | N | N | N | NA | N | N |
| **Rash** | N | N | N | N | N | N | N | N | N | N | N | N | N |
| **Muscle aches** | N | NA | N | N | N | NA | N | N | N | N | NA | N | N |
| **Loss of smell or taste** | Until day 11 | NA | N | N | N | NA | N | N | N | N | NA | N | N |
| **COVID related hospitalization** | N | N | N | N | N | Until day 7 | N | N | N | N | Until day 23 | N | N |
| **Need for supplemental oxygen** | N | N | N | N | N | Until day 7 | N | N | N | N | Until day 15 | N | N |
| **Need for non-invasive positive pressure ventilation** | N | N | N | N | N | Until day 5 | Back to baseline at day 7 | N | N | N | Until day 6 | N | N |
| **[1]SARS-CoV-2 NP RT-PCR** | Neg at day 14 | Neg at day 7 | Neg | Pos at day 12 and 21 | N | Missing data | Neg at day 34 | N | | | | | |

[1]See Supplemental Figure 1B for additional details. NA – non-applicable.




[1]Primary or acquired immunodeficiency e.g. recipient of a bone marrow or solid organ transplant in the last 12 months (or at any time if concurrent with graft-versus host disease), recipient of chemotherapy for a malignancy within the past 6 months, HIV with CD4 (<30% for ≤12 months old; <25% for 12–35 months; <20% for 36–59 months or <350 for all other ages), receiving immunosuppressive or immunomodulatory treatments (e.g., high-dose steroids [≥2 mg/kg/day of systemic prednisone or equivalent for ≥14 days], tacrolimus, sirolimus, cyclosporine, antithymocyte globulin - ATG, mycophenolate, methotrexate, etc.)

[2]Defined as children who has long-term dependence on technological support (including tracheotomy) associated with developmental delay and/or genetic anomalies (Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. *JAMA Pediatrics* 2020

[3]Hemodynamically significant cardiac disease (e.g., congenital heart disease)

[4]Lung disease with chronic respiratory failure (e.g., patients with asthma, cystic fibrosis, bronchiectasis, chronic lung disease of prematurity, tracheostomy / ventilator dependency, restrictive lung disease, severe neuromuscular disease, etc.)

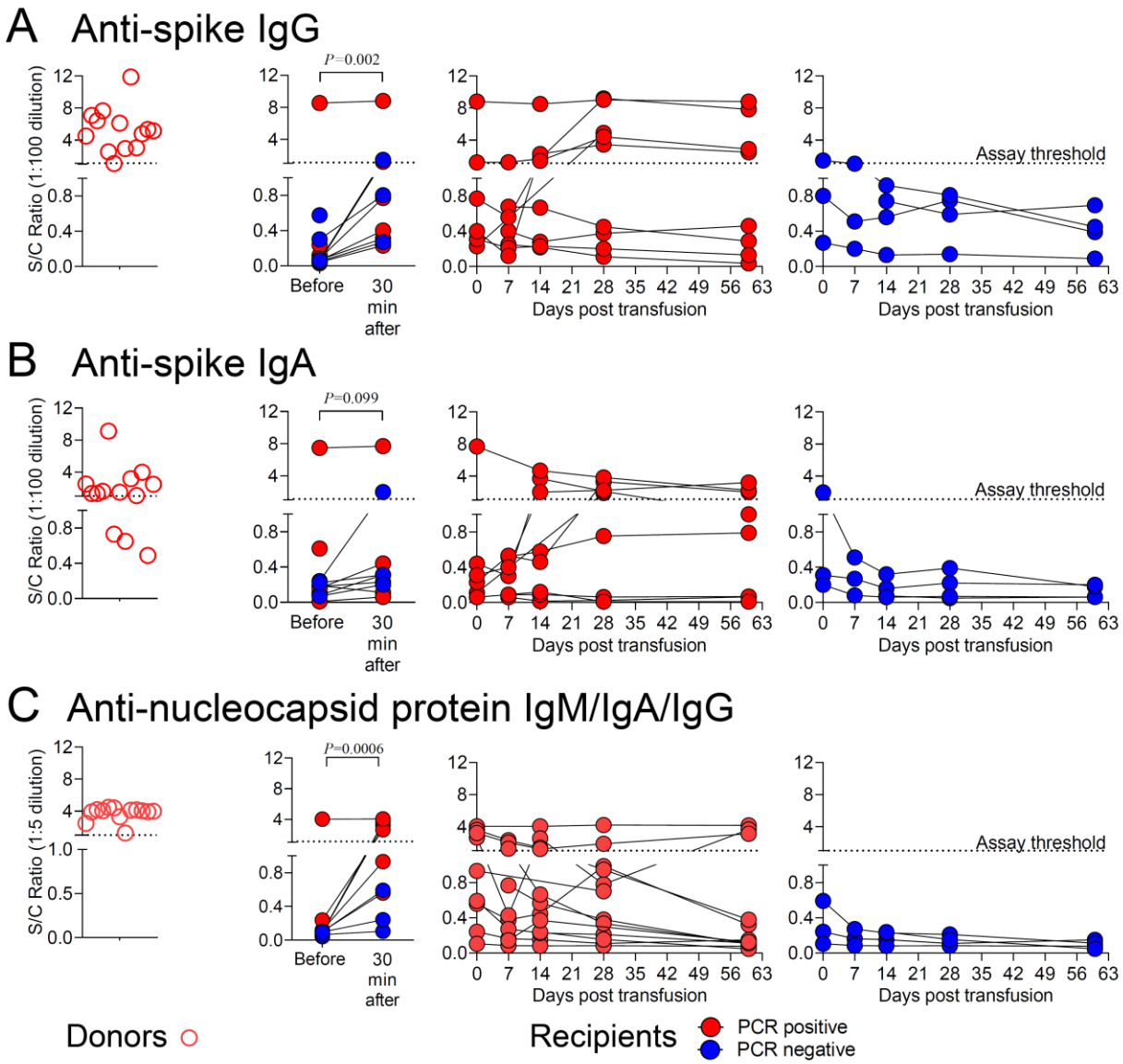
[5]Defined as a body mass index (BMI) ≥95$^{th}$ percentile for children and teens of the same age and sex (CDC. "Defining Childhood Obesity" https://www.cdc.gov/obesity/childhood/defining.html. 2018; 3 July. CDC. "People with Certain Medical Conditions" https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html 2020; 30 July).

[6]CDC. Coronavirus Disease 2019 in Children — United States, February 12–April 2, 2020. *https://wwwcdcgov/mmwr/volumes/69/wr/mm6914e4htm?s_cid=mm6914e4_e&deliveryName=USCDC_921-DM25115* 2020.

[7]Dong Y, Mo X, Hu Y, et al. Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics* 2020: e20200702.

[8]All criteria below should be met

**Supplementary Figure 1. Eligibility criteria**

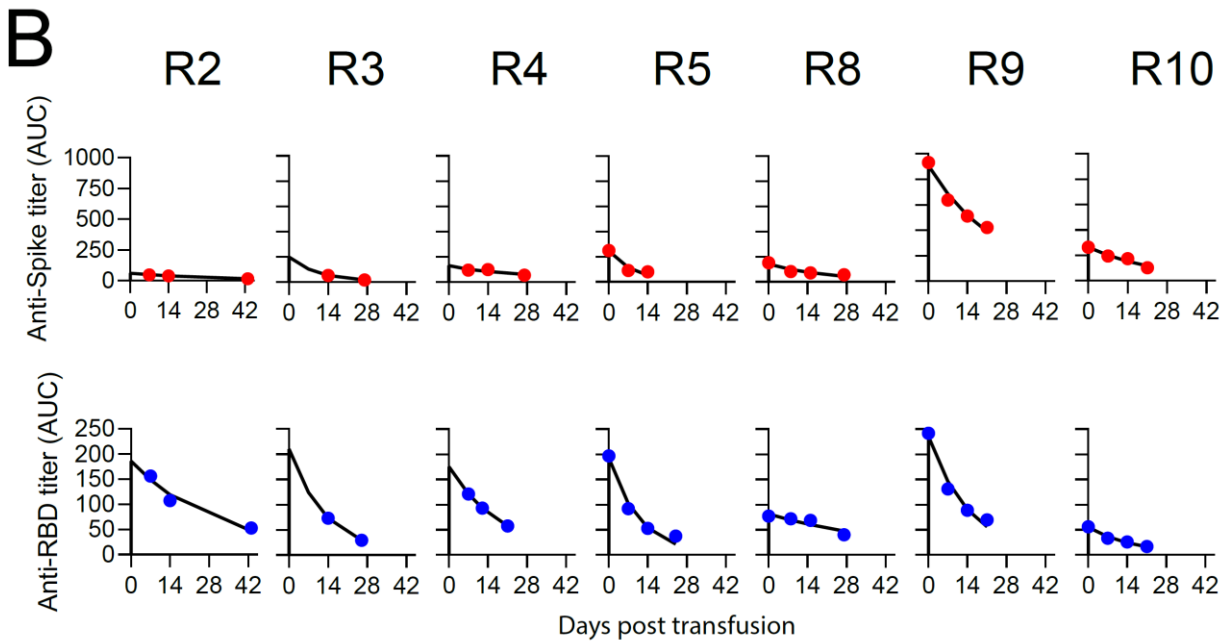



**Supplementary Figure 2. Antibody titers in donors and recipient plasma measured by commercial assays.** Results presented as signal to cut-off ratio (S/C). Recipients are graphed separately based on SARS-CoV-2 positivity, with those PCR negative (blue) on far right. Anti-spike IgG (**A**) and IgA (**B**) antibodies measured by ELISA (Euroimmun, Lubeck, Germany). Y-axes are segmented to demonstrate the manufacturer recommended assay thresholds: negative (S/C ratio < 0.8), borderline, (S/C ratio ≥0.8 & <1.1) or positive (S/C ratio ≥1.1). (**C**) Anti-nucleocapsid (N) IgM/IgA/IgG measured using EIA (BioRad Platelia, Marnes-la-Coquette, France). Y-axes are segmented to demonstrate the manufacturer recommended assay thresholds: negative (S/C ratio < 0.8), borderline, (S/C ratio ≥0.8 & <1.0) or positive (S/C ratio ≥1.0). For all assays, n=13 pairs of donors and recipients. A two-tailed Mann-Whitney U test was used to compare donor to recipient titers and recipient titers before and 30 minutes after transfusion. The corresponding *p*-values are shown.

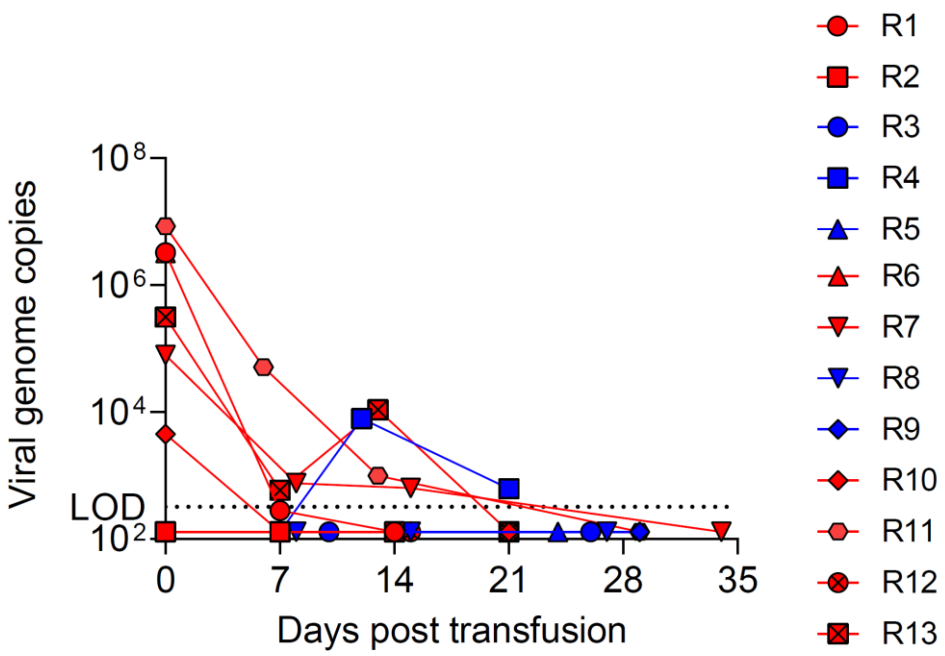
A Summary of PK analysis

| | Weight (kg) | Anti-Spike IgG | | Anti-RBD IgG | |
|---|---|---|---|---|---|
| | | CL (AUC/day) | $T_{1/2}$ (days) | CL (AUC/day) | $T_{1/2}$ (days) |
| R2 | 4.49 | 1.05 | 22.9 | 0.74 | 21.5 |
| R3 | 13.8 | 0.77 | 7.3 | 1.1 | 9.2 |
| R4 | 64.3 | 1.68 | 18.6 | 0.98 | 13 |
| R5 | 65.8 | 1.73 | 6.3 | 2.05 | 7.6 |
| R8 | 49.1 | 0.86 | 15.5 | 0.73 | 34.3 |
| R9 | 16.4 | 3.24 | 17.2 | 0.49 | 10.1 |
| R10 | 19.1 | 0.67 | 17.7 | 0.49 | 11.8 |

B




**Supplementary Figure 3. Pharmacokinetic (PK) analysis of antibody titers in recipients.** **(A)** Model predicted PK characteristics. Clearance (CL) and half-life ($T_{½}$) of anti-spike and anti-RBD IgG were estimated using two stage analysis. (**B**) Individual predictions of anti-spike and anti-RBD IgG from PK analysis. Red and blue dots represent the observed titers and black lines present the predicted time course of titers.




**Supplementary Figure 4. Quantitative SARS-CoV-2 PCR.** Nasopharyngeal swabs were taken on the day of and weekly following plasma administration for up to 4-5 weeks. Viral genome copies are shown for each recipient (red for PCR-positive and blue for PCR-negative). For recipients R2 and R12, a clinical (non-quantitative) SARS-CoV-2 PCR was positive at day 0. LOD – limit of detection.