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Convalescent plasma transfusion for immunocompromised viremic patients with COVID-19: A retrospective multicenter study

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Abstract

This study aims to assess the safety, virological, and clinical outcomes of convalescent plasma transfusion (CPT) in immunocompromised patients hospitalized for coronavirus disease 2019 (COVID-19). We conducted a retrospective multicenter cohort study that included all immunosuppressed patients with COVID-19 and RNAemia from May 2020 to March 2023 treated with CPT. We included 81 patients with hematological malignancies (HM), transplants, or autoimmune diseases (69% treated with anti-CD20). Sixty patients (74%) were vaccinated, and 14 had pre-CPT serology >264 BAU/mL. The median delay between symptom onset and CPT was 23 days [13–31]. At D7 post-CPT, plasma PCR was negative in 43/64 patients (67.2%), and serology became positive in 25/30 patients (82%). Post-CPT positive serology was associated with RNAemia negativity ($p < 0.001$). The overall mortality rate at D28 was 26%, being higher in patients with non-B-cell HM (62%) than with B-cell HM (25%) or with no HM (11%) ($p = 0.02$). Patients receiving anti-CD20 without chemotherapy had the lowest mortality rate (8%). Positive RNAemia at D7 was associated with mortality at D28 in univariate analysis (HR: 3.05 [1.14–8.19]). Eight patients had adverse events, two of which were severe but transient. Our findings suggest that CPT can abolish RNAemia and ameliorate the clinical course in immunocompromised patients with COVID-19.

KEYWORDS

combination therapy, disease control, infection, SARS coronavirus, virus classification

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1 | INTRODUCTION

In December 2019, a new coronavirus was identified in Wuhan, China. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), spread rapidly worldwide and led to an unprecedented health crisis.

Immunocompromised patients, who are unable to benefit from the protection provided by vaccination, have a higher risk of severe or protracted COVID-19.¹ Such is the case for patients with hematological malignancies (HM), especially those treated with anti-CD20; indeed, a meta-analysis indicated that such patients have a 32% fatality rate.² However, to date, there is no recommended treatment strategy for this population.³ Antivirals, immunomodulators, and anti-inflammatories are recommended for patients in the active phase of COVID-19.⁴⁻⁷ Direct antivirals are used for COVID-19 treatment but have low clinical efficacy⁸ and carry the risk of drug-drug interaction (nirmatrelvir-ritonavir) in this heavily treated population. The use of anti-inflammatory drugs (dexamethasone, tocilizumab, and baricitinib) may be counterintuitive in immunosuppressed patients.⁵⁻⁷ Monoclonal antibodies (mAbs) were effective in seronegative patients, but the loss of efficacy against SARS-CoV-2 subvariants is a concern.⁹

Convalescent plasma therapy (CPT) relies on passive immunotherapy as a curative treatment for COVID-19 and involves transfusion of plasma from immunized donors. The mechanism of action is dependent on polyclonal anti-SARS-CoV-2 antibodies targeting the spike protein, which exert a direct antiviral effect (including interference with the receptor-binding domain), and promote viral clearance via immunoglobulin-mediated neutralization and other mechanisms (i.e., phagocytosis, cytotoxicity, and complement activation).¹⁰ Moreover, anti-inflammatory cytokines, clotting factors, and natural antibodies are obtained via transfusion, potentially improving inflammation.¹¹

Although several trials showed no benefit in the general population,^{12,13} a recent randomized control trial showed better survival among intubated unvaccinated immunocompetent patients in the ICU when administered early after intubation.¹⁴ The trial was conducted early in the pandemic, among patients who did not benefit from antivirals or immunomodulators. Observational studies and clinical trials suggest its potential in immunocompromised patients, especially with HM, for acute or protracted COVID-19.¹⁵⁻¹⁹ However, these studies did not evaluate a virological endpoint, including SARS-CoV-2 in the blood (RNAemia), to assess the ability of CPT to enhance viral clearance.

We report the results of a retrospective multicenter observational cohort study of the clinical, virological, and safety outcomes of CPT in immunocompromised patients hospitalized for moderate to critical COVID-19 with RNAemia.

2 | MATERIALS AND METHODS

2.1 | Study design

This observational retrospective multicenter cohort study was conducted in eight hospitals in six cities in the Nouvelle-Aquitaine region of France.

On April 29, 2020, the French national authorities authorized the collection and use of convalescent plasma as part of a therapeutic-use protocol. Following this decision, a multidisciplinary team meeting (CPT team) was organized in St-André University Hospital, Bordeaux. The meeting involved intensivists, infectious disease specialists, and French regional blood establishment referral physicians, with a view to allocating plasma in the Nouvelle-Aquitaine region.

Between May 2020 and March 2023, the French Blood Establishment carried out 125 CPT deliveries, which were validated by the CPT team. This study included only immunosuppressed patients (patients with HM, autoimmune disease, solid organ transplantation, or active solid cancer; or receiving chemotherapy or other immunosuppressive treatment), hospitalized with COVID-19 (WHO score ≥ 4) with positive RNAemia before CPT.

Plasma was collected from convalescent donors (moderate COVID-19 1-6 months before donation) who were treated according to the Intercept[®] Amotosalen technique. Patients provided written informed consent and received an average of 4 units of CPT (i.e., around 800 mL), in two or four transfusions at 24 h intervals. Convalescent plasma titers were 80 to >7000 BAU/mL (high-titer CP) during the study period.

2.2 | Data collection

The following clinical parameters were collected at baseline, during hospitalization, and follow-up: age, sex, body mass index, comorbidities, 2011 revised Charlson score,²⁰ immunosuppressive disease and treatment, COVID-19 vaccination, and pre-CPT treatment. Clinical status was evaluated by calculating the 10-point World Health Organization (WHO) clinical score.²¹

The WHO score, biological parameters, and virological parameters (SARS-CoV-2 RNAemia and serology) were collected at baseline (D0, before CPT), D3 (D2-D4), D7 (D5-D9), D14 (D12-D16), and D28 (D26-D30). Chest computed tomography was conducted to quantify the severity of lung damage at baseline. Among patients in intensive care units (ICU), the IGS2 and SOFA scores were determined at baseline. The causes of clinical worsening and deaths and the need for additional treatments were recorded.

RNAemia was evaluated using the COVID-19 R-GENE (BioMérieux) until April 2022, and the Cobas[®] SARS-CoV-2 Kit (Roche Diagnostics) thereafter. Thus, the viral targets differed over time (nucleocapsid [N], RNA-dependent RNA polymerase [RdRp], and Envelope [E] for R-GENE and E and ORF-1 for Cobas). Cycle threshold (CT) values ≤ 40 were considered positive results. SARS-CoV-2 serology was reported as binding antibody units/mL, as recommended by the WHO. A titer of >264 BAU/mL was considered positive.²²

2.3 | Outcomes and statistical analysis

The primary outcome was survival at D28, defined as the time between CPT administration and all-cause death. The secondary

TABLE 1 Baseline characteristics before CPT (D0).

Patients' characteristics (N = 81)	N = 81 ^a
Age (years, median [IQR])	69 [61–75]
Gender female (n, %)	23 (28.4%)
Comorbidities (n, %)	
Hypertension	35 (43.2%)
Diabetes	16 (19.8%)
Chronic renal failure	17 (21.0%)
Chronic heart failure	12 (14.8%)
Obesity	10 (12.3%)
≥1 comorbidity other than immunodepression	47 (58.0%)
Acquired immunosuppression (n, %)	
Hematologic malignancies (HM)	64 (79.0%)
B-cell HM	56 (69.1%)
Non-B-cell HM	8 (9.8%)
Solid organ transplant	8 (9.90%)
Autoimmune disease	11 (13.6%)
Immunosuppressive treatment (n, %)	
Anti-CD20 + other chemotherapy	31 (38.3%)
Anti-CD20 without other chemotherapy	25 (30.9%)
Other chemotherapy alone	13 (16.0%)
Anti-rejection treatment	9 (11.1%)
Long-term corticosteroids	24 (29.6%)
Others	9 (11.1%)
Previous COVID-19 treatment (n, %)	
Vaccinated (≥1 dose)	60 [74.1%]
No of previous vaccines (median [IQR])	3 [0–3]
mAbs (tixagevimab/cilgavimab) <6 months	19 (23.5%)
Treatment received before CPT	
Corticosteroids	74 (91.4%)
Tocilizumab	37 (45.7%)
Nirmatrelvir/ritonavir	19 (23.5%)
Other treatments	4 (4.9%)
Clinical characteristics	
Days between symptom onset and CPT (median [IQR])	23 [13–31]
WHO score ≥6 (D0)	44 (54.3%)
Fever	55 (67.9%)
CT-scan pulmonary damage >50%	42 (53.2%)
Biological characteristics (median [IQR])	
Lymphocytes (G/L)	0.38 [0.18–0.53]

TABLE 1 (Continued)

Patients' characteristics (N = 81)	N = 81 ^a
Neutrophil count (G/L)	3.8 [2.2–6.6]
CRP (mg/L)	99 [51–153]

Abbreviations: COVID-19, coronavirus disease 2019; CPT, convalescent plasma transfusion; CRP, C-reactive protein; CT, computed tomography; D0, day 0 before plasma; ICU, intensive care unit; IQR, interquartile range; mAbs, monoclonal antibodies; WHO, World Health Organization.

^a(n [%]; median [IQR]).

outcomes were clinical and biological evolution between CPT (D1) and D28, and the adverse effects of CPT.

Survival curves were plotted by the Kaplan–Meier method against predefined subgroups and compared by log-rank tests. To identify factors associated with all-cause death, Cox models were used to estimate hazard ratios (HR) and 95% confidence intervals (CIs). HRs for each factor of interest were estimated crude (univariate) and adjusted for the following variables (multivariate): age, sex, WHO score at inclusion (≥ or <6), and type of immunosuppression (B-cell HM, other HM, or no HM).

To identify factors associated with the persistence of viremia at D7 of CPT administration, only patients with an available blood PCR result at D7 were analyzed. Logistic regression models were used to estimate odds ratios (ORs) and 95% CIs for each factor of interest, crude (univariate), and adjusted for predefined variables (multivariate). Other exploratory analyses were conducted using the χ^2 or Fisher test (qualitative variables) and the Wilcoxon test (quantitative variables).

A two-tailed *p*-value < 0.05 was considered indicative of statistical significance. The proportionality of the instantaneous risk of death in the Cox models was verified by the Schoenfeld residual method. The linearity of quantitative variables was verified using cubic splines. No imputation of missing data was performed, given the small number of missing data. Analyses were carried out using R studio (version 1.1.463; R Development Core Team) and the survival, survey, and cobalt packages.

3 | RESULTS

3.1 | Population characteristics at baseline

We analyzed 81 patients, among whom 28% were women; the median age was 69 years (IQR [61–75]) (Table 1). Thirty-eight patients were hospitalized in medical wards and 43 in the ICU; all received at least one dose of CPT (Supporting Information Material 1). Among HM, 56 were B-cell HM (20 follicular lymphomas, 9 mantle cell lymphoma, 9 chronic lymphocytic leukemias, 11 diffuse large B-cell lymphomas, 7 others), and 8 were non-B-cell HM (4 multiple myelomas, 2 acute leukemias, 1 mycosis fungoid, 1 VEXAS syndrome). Other causes of immunodepression were 11 autoimmune diseases, 8 solid organ transplants, and 1 solid cancer. All the patients received immunosuppressive treatment, and 56

(69%) had received anti-CD20 < 12 months before CPT. Most patients (74%) were vaccinated. At baseline, before CPT only 14 had positive SARS-CoV-2 serology, 11 of whom had received mAbs (tixagevimab/cilgavimab). Among the ICU patients at D0, the median IGS2 and SOFA scores were 43 [38–49] and 3 [3–6] respectively; 69% had a PaO₂/FiO₂ < 200.

3.2 | Clinical evolution after CPT

The overall mortality rate at D28 was 21 of 81 patients (25.9%) (Table 2). The main cause of death was COVID-19 for 10 patients

TABLE 2 Clinical evolution after CPT (between D1 and D28).

Patients' clinical evolution (N = 81)	N = 81 ^a
Median hospital stay (days)	
ICU	7 [3–16]
Medical wards	11 [6–18]
Characteristics at D28	
Fever	0 (0%)
WHO score	
Ambulatory, uninfected	51 (62.9%)
Hospitalized: moderate disease	5 (6.2%)
Hospitalized: severe disease	4 (4.9%)
Dead	21 (25.9%)
Negativation of RNAemia between D1 and D28 ^b	66 (83%)
Cause of clinical worsening ^c	35 (43%)
Pneumonia (bacterial, fungal)	22 (59%)
Worsening of COVID-19	19 (51%)
Cardiovascular events ^d	15 (42.8%)
Worsening of HM	8 (22.8%)
Other infections	2 (2.5%)
Deaths	21 (25.9%)
No days between D0 and death	12 [9–18]
Main cause of death	
COVID-19	10 (47.6%)
Stroke or hemorrhage	2 (9.5%)
Worsening of hematologic malignancy	3 (14.3%)
Other infections	6 (28.6%)

Abbreviations: COVID-19, coronavirus disease 2019; CPT, convalescent plasma transfusion; HM, hematological malignancies; ICU, intensive care unit; WHO, World Health Organization.

^a(n [%]; median [IQR]).

^bAmong patients with available blood PCR after D0 (n = 79).

^cSometimes several causes per patient.

^dNine cardiac decompensations, one stroke, four pulmonary embolisms, and one hemorrhage.

(47.6%). Among survivors at D28 (n = 60), 51 (85%) had a WHO clinical score of 0 (ambulatory, uninfected) (Figure 1). Between D1 and D28, 83.5% (66/79) of patients with available PCR did not have RNAemia. Nine of the 10 patients with persistent RNAemia after D7 (D14–D28) died.

Six patients (all with WHO scores ≥ 6 at D0) had a second CPT (dose 2–8 units) with a median delay of 7 days (4–10 days) because of RNAemia persistence. RNAemia became undetectable in five of the six patients, one of whom died. The patient with persistent RNAemia died. Eight patients experienced a side-effect of CPT according to the definitions of the French National Authority for Health²³: seven cardiovascular events (hypertension, dyspnea), and one cutaneous eruption. Two were severe and required increased oxygen and intubation; these occurred in patients in the ICU with multiple comorbidities (one cardiac transplant with heart failure and severe coinfections, one with bi-pulmonary transplant and severe chronic renal failure) and were rapidly resolved.

3.3 | Factors associated with all-cause mortality

The overall mortality rate at D28 was higher in patients with non-B-cell HM (62%) than with B-cell HM (25%) or no hemopathy (11%) (p = 0.02). Patients on anti-CD20 without other chemotherapy had the lowest mortality rate (8%) (Table 3). Survival curves according to WHO score and type of immunosuppression are shown in Figure 2.

In univariate and multivariate analyses, severe disease (WHO score ≥ 6) at D0 (before CPT) was associated with a higher risk of mortality (HR: 17.33 [CI: 2.26–132.69]). HM (vs. SOT or autoimmune diseases) was associated with increased mortality, particularly non-B-cell HM (HR: 6.3 [CI: 1.2–33.03]). Regarding immunosuppressives, anti-CD20 plus chemotherapy and other modalities (i.e., chemotherapy alone, long term corticosteroids, or anti-rejection treatment) were associated with mortality when compared to patients only on anti-CD20 (respectively HR: 5.34 [CI: 1.58–24.08] and HR: 4.93 [CI:

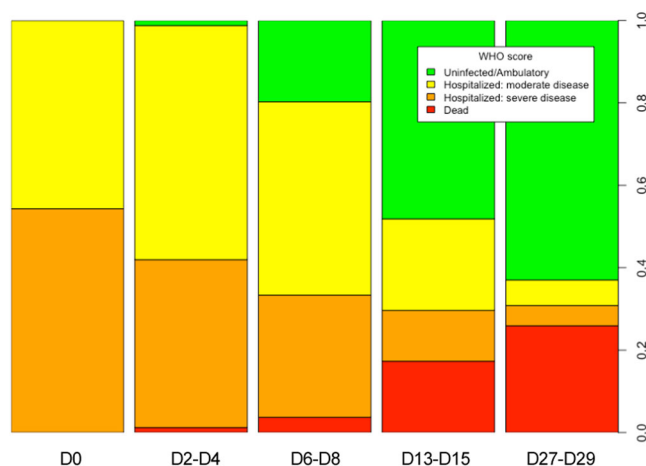


FIGURE 1 Evolution of WHO score between D0 and D28 (CPT administration at D1). CPT, convalescent plasma transfusion.

TABLE 3 Risk factors associated with all-cause mortality.

Risk factors associated with mortality	Univariate analysis		Multivariate analysis ^a	
	HR	95% CI	HR	95% CI
Age (for each year older)	1.04	(1.00–1.09)	1.07	(1.01–1.14)
Male versus female sex	1.42	(0.52–3.87)	1.5	(0.54–4.17)
Severe versus moderate disease ^b	16.18	(2.14–122.13)	17.33	(2.26–132.69)
Versus no HM (ref)	1 (ref)		1 (ref)	
B-cell HM	2.39	(0.54–10.54)	1.4	(0.29–6.77)
non-B-cell HM	8.19	(1.58–42.44)	6.3	(1.20–33.03)
Charlson ^c ≥3 versus < 3	0.87	(0.34–2.25)	0.55	(0.19–1.59)
Hypertension	1.94	(0.82–4.61)		
Diabetes	2.64	(1.06–6.55)	2.92	(0.99–8.58)
Chronic renal failure	1.71	(0.66–4.40)		
Chronic cardiac failure	2.09	(0.77–5.71)		
Undernutrition	1.13	(0.38–3.35)		
Obesity	1.29	(0.38–4.39)		
Vaccine ≥3 versus <3 doses	0.67	(0.28–1.6)		
mAbs within 6 months	1.02	(0.37–2.79)		
Days between symptom onset and CPT: (for each day more)	0.96	(0.92–1.00)	0.97	(0.93–1.01)
Days between symptom onset and CPT: ≤10 versus >10 days	2.54	(1.02–6.31)	2.41	(0.89–6.52)
Tocilizumab before CPT	2.01	(0.83–4.85)		
Nimratrelvir/ritonavir before CPT	0.14	(0.02–1.00)	0.17	(0.02–1.29)
In ICU patients: IGS2 (for each +10 points)	1.33	(0.83–2.14)		
In ICU patients: SOFA (for each +2 points)	1.25	(0.88–1.78)		
Fever	1.13	(0.43–2.98)		
CT-scan lung injury ≤50% versus >50%	0.31	(0.11–0.85)	0.59	(0.19–1.80)
Pulmonary embolism at baseline	3.72	(0.49–27.94)		
Lymphopenia at baseline (for each +0.1 G/L)	2.73	(0.5–14.84)		
Neutrophil count at baseline (for each +0.1 G/L)	2.24	(0.79–6.34)		
CRP (for each +30 mg/L)	1.05	(0.89–1.24)		
Plasma adverse event versus none	2.35	(0.79–7.00)		
Blood RNAemia positive at D7 ^e	3.05	(1.14–8.19)	1.22	(0.42–3.57)
IgG anti-S ≥ 264 BAU/mL before D7 ^f	0.33	(0.06–1.99)		

Note: Results in bold are statistically significant.

Abbreviations: 95% CI, confidence interval; BAU/mL, international units for COVID-19 serology; COVID-19, coronavirus disease 2019; CPT, convalescent plasma transfusion; CRP, C-reactive protein; CT, computed tomography; D1, first day of CPT administration; HM, hematological malignancies; HR, hazard ratio for all-cause mortality; ICU, intensive care unit; mAbs, monoclonal antibodies (tixagevimab/cilgavimab).

^aMultivariate analysis adjusted for age, sex, severity, and HM.

^bSevere is a WHO score ≥6.

^cCharlson score revised version (Quan et al.²⁰).

^dAmong those alive and with available PCR at D7 (n = 64).

^eAmong those living and with available serology at D6–D8 who were previously negative for mAbs (n = 34).

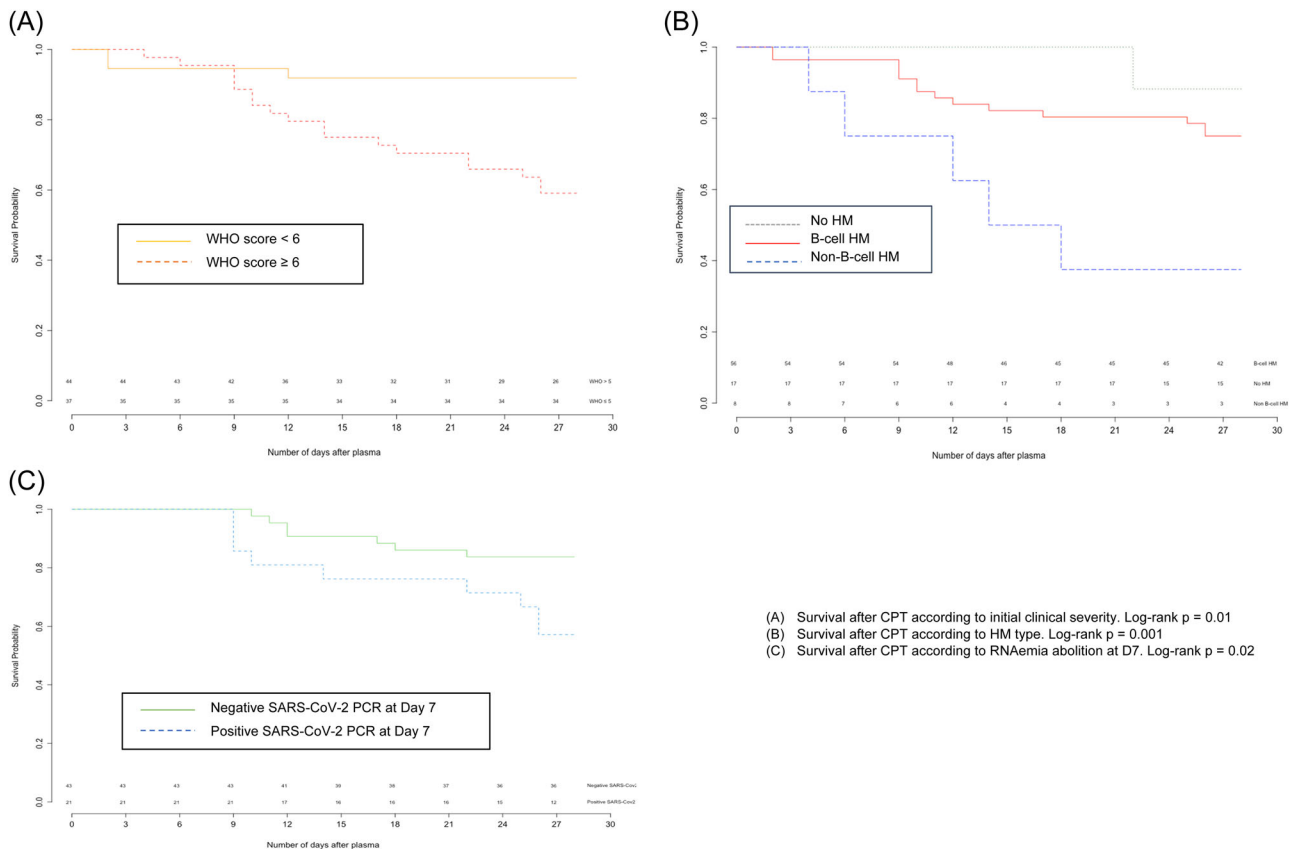


FIGURE 2 Survival curves according to WHO score (A), type of immunosuppression (B), and RNAemia (C).

1.05–23.23]). Among patients with available plasma PCR at D7 post-CPT ($n = 65$), persistent RNAemia at D7 was strongly associated with mortality (HR: 3.05 [CI: 1.14–8.19]) in a univariate analysis. Survival curves according to RNAemia are shown in Figure 2.

Nirmatrelvir/ritonavir was received by 19 patients (in 17 within 48 h before CPT). They showed less clinical worsening during follow-up (16% vs. 53%, $p = 0.004$) and nonsignificantly lower mortality (HR: 0.14 [CI: 0.02–1.00]); only one died.

3.4 | RNAemia evolution after CPT

At D7, among 65 patients with available plasma PCR, 21 had persistent RNAemia. Clinical severity (WHO ≥ 6) at D0 was significantly associated with persistent RNAemia at D7 in a multivariate analysis (HR: 6.6 [CI: 1.84–23.7]). After April 12, 2022, RNAemia was monitored using the Cobas® SARS-CoV-2 Kit. For 24 patients with at least one available PCR between D3 and D28 using the Cobas kit, the evolution of viremia using E and ORF-1 as targets is shown in Figure 3.

3.5 | Relationship between serology, RNAemia, and clinical outcomes

Among the 58 patients seronegative at baseline, 30 had another serology between D1 and D7. Seroconversion (i.e., serology ≥ 264

BAU/mL) before D7 ($n = 25$) was associated with absence of RNAemia at D7 ($n = 21$) ($p < 0.001$; Fisher test). None of the five patients with no seroconversion before D7 had negative RNAemia at D7. Seroconversion before D7 was associated with a shorter hospitalization duration ($p < 0.05$) but not with mortality ($p = 0.2$). Serology monitoring among patients without previous mAbs showed initial seroconversion followed by a rapid decrease during follow-up (Figure 4).

4 | DISCUSSION

We report an overall mortality rate of 25.9% at D28 after CPT in immunocompromised patients with COVID-19. The overall mortality rate was significantly higher in patients with non-B-cell HM (62%) and B-cell HM (25%) than with no HM (11%). Patients on anti-CD20 without chemotherapy had the lowest mortality rate (8%). After CPT, 67% of patients lost RNAemia, and 82% seroconverted at D7. Persistent RNAemia at D7 was strongly associated with baseline clinical severity (WHO ≥ 6) and mortality at D28.

This study is the first of RNAemia and serology in immunocompromised patients receiving CPT. Our results are consistent with prior reports on the association of SARS-CoV-2 viremia and its persistence with severity and mortality,²⁴ and of that between seroconversion and viral clearance.²⁵ This strong association between RNAemia and clinical severity emphasizes the importance

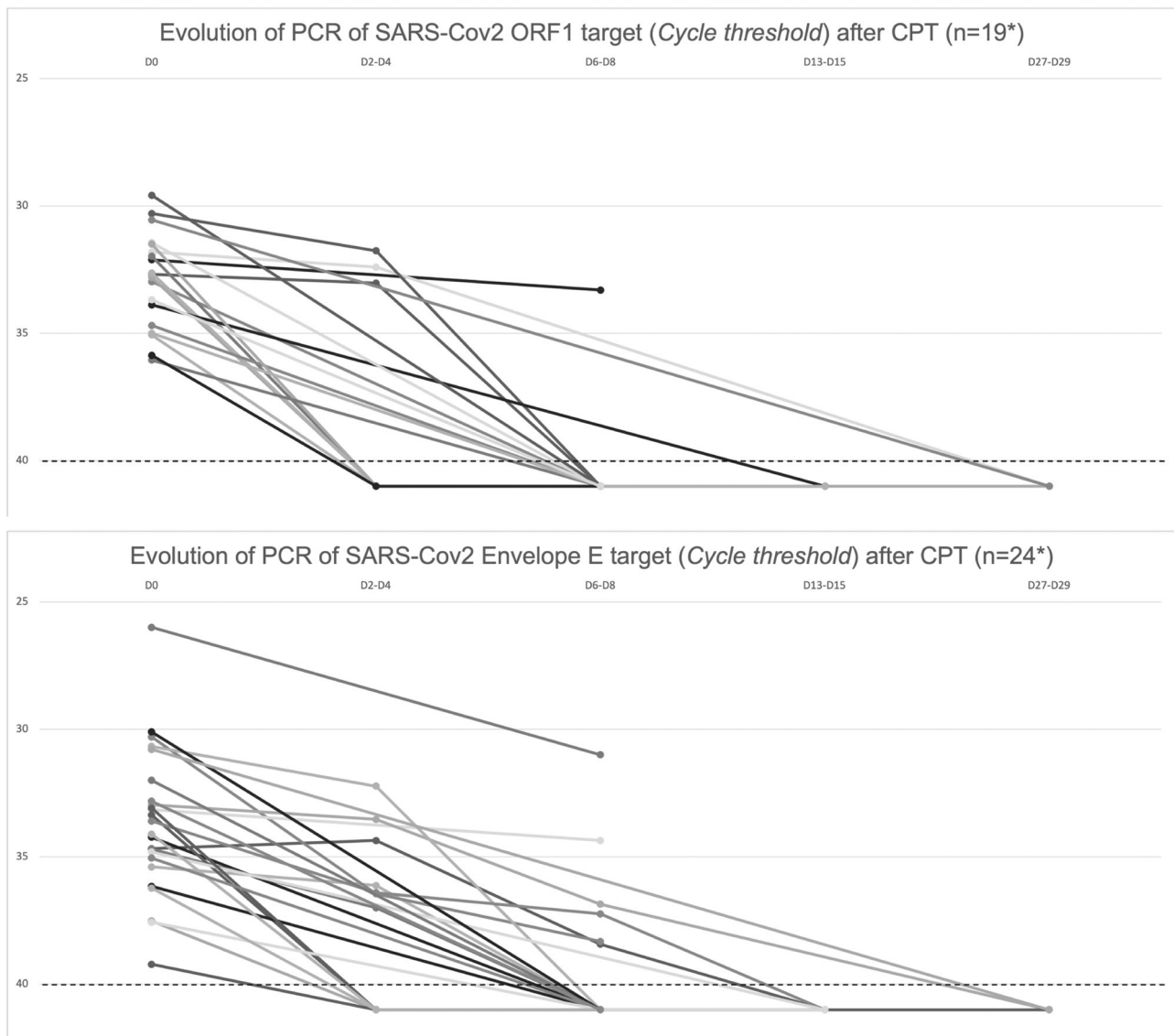


FIGURE 3 Evolution of RNAemia after CPT. *Among patients with at least two repeated C_t values using the same PCR technique (E and ORF1 as targets) from April 2022 to March 2023. CPT, convalescent plasma transfusion.

of rapid viral neutralization. The long time from symptoms onset to CPT (median 23 days) confirms the longer time of viral replication in immunocompromised patients with often prolonged phase of moderate symptoms before worsening. In this study, RNAemia C_t -values increased until lack of detection after CPT. Nasopharyngeal PCR swabs monitoring, with sometimes long-lasting positivity despite clinical resolution, was less effective and related to clinical evolution than RNAemia.²⁶

CPT reportedly benefits immunocompromised patients with acute or protracted COVID-19, particularly those with humoral immunodepression.^{15,16,18} A meta-analysis of immunocompromised patients receiving CPT or standard-of-care showed a lower mortality in the CPT group.¹⁷ In association with CPT, antiviral treatment can optimize viral shedding. In this study, patients receiving nirmatrelvir/ritonavir showed less clinical worsening and nonsignificantly lower mortality. This could be

because of a lack of power or the fact that patients on medical wards more frequently received nirmatrelvir/ritonavir than those in the ICU (37% vs. 14%). This treatment was authorized in France in January 2022; hence it was evaluated only for patients in the last year of the study and. Before CPT, 92% of patients received anti-inflammatory drugs such as corticosteroids and tocilizumab. These therapies could suppress the cytokine storm induced by COVID-19 but not RNAemia. Clearance is fundamental for immunocompromised patients, given that low viral loads can lead to symptomatic relapse.

This study has several strengths. It was a multicenter study and evaluated clinical outcomes in hospitalized severely immunocompromised patients, who do not fully benefit from vaccination. We developed a standardized procedure for collecting clinical and biological data in multidisciplinary team meetings. This is the first study to monitor RNAemia in patients receiving CPT.

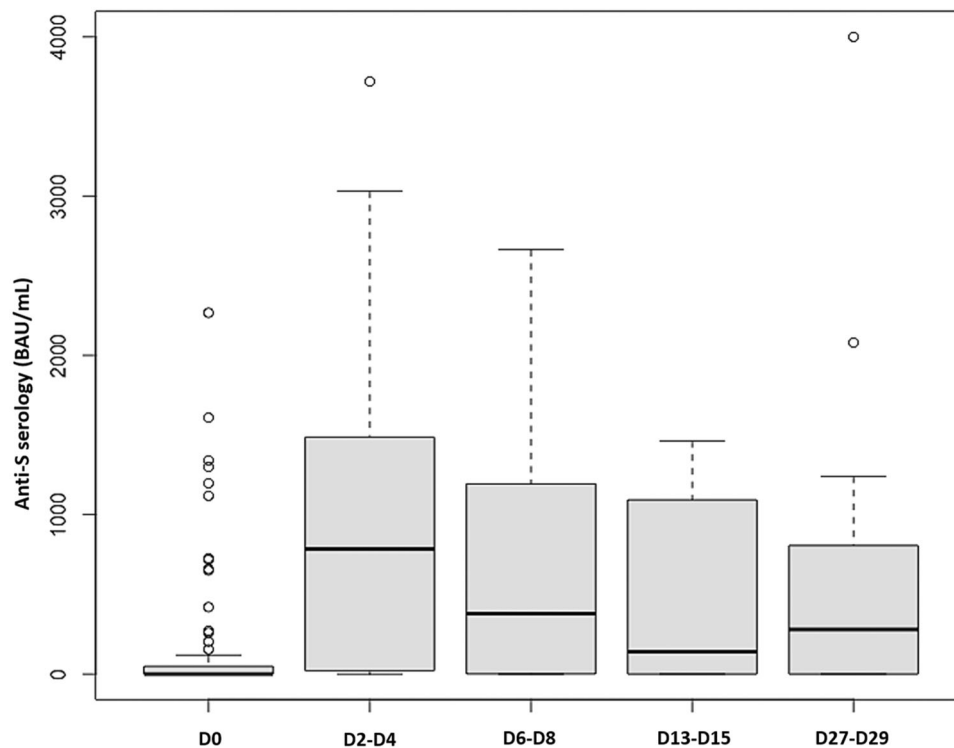


FIGURE 4 Evolution of SARS-CoV-2 serology after CPT among patients without previous monoclonal antibody (mAbs). CPT, convalescent plasma transfusion; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

This study also has limitations. It was a retrospective, non-comparative study, and therefore it is possible that clinical improvement and viral clearance were a result of other treatments or the natural evolution of the infection. The number of patients was insufficient to envisage a precise target population. Missing data for clinical characteristics were scarce, but numerous for serology; therefore, analysis on serology is at risk of selection bias. Convalescent plasma titers were 80 to >7000 BAU/mL during the study period, but transfusion of 4 CPT units potentially reduces the risk of an insufficient antibody titer.²⁷ The seroconversion threshold (>264 BAU/mL), which is commonly used, may not be relevant for Omicron variants of SARS-CoV-2.²⁸

Given the high mutation rate and the ineffectiveness of mAbs, CPT (if collected recently) reflects the current circulating variants and the polyclonal immune response of several donors. Our data suggest its safety, as did prior work.²⁹

Our findings suggest viremic seronegative immunocompromised patients, hospitalized with noncritical and/or persistent COVID-19, as the target population. For ICU patients, CPT should be administered as early as possible to abolish RNAemia before clinical worsening. RNAemia and serology monitoring enable assessment of efficacy. Our findings support a link between seroconversion and RNA undetectability, but serologic positivity was not prolonged, possibly due to antibody consumption. This suggests the need for higher titer CPT, which has increased efficacy against the most recent Omicron variants.³⁰ Repeated CPT administration could be effective in patients with persistent RNAemia.

5 | CONCLUSION

Our findings suggest that CPT reduces RNAemia and ameliorates the clinical course in viremic seronegative immunocompromised patients with COVID-19, particularly those with humoral immunosuppression. Comparative studies are necessary to confirm this hypothesis and formulate a treatment strategy.

AUTHOR CONTRIBUTIONS

Marjolaine Destremau, H el ene Chaussade, Mathilde Beguet, Pantxika Bellecave, Elodie Blanchard, Amaury Barret, Gaelle Laboure, Claire Vasco-Moyne, Flore Lacassin, Elo ise Morisse, Claire Aguilar, Nah ema Issa, and Fabrice Camou collected the data. Marjolaine Destremau, H el ene Chaussade, Victor Hemar, Mathilde Beguet, Pantxika Bellecave, Xavier Lafarge, Marie-Edith Lafon, Fabrice Bonnet, Nah ema Issa, and Fabrice Camou designed the research study and analyzed the data. Victor Hemar developed the statistical analysis. Marjolaine Destremau, H el ene Chaussade, Victor Hemar, Fabrice Bonnet, Nah ema Issa, and Fabrice Camou wrote the paper. All authors have read and approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Patients provided written informed consent before receiving CPT. Handling of the data for retrospective research purposes was declared to the Data Protection Officer and approved by the Ethical Committee of the University Hospital of Bordeaux (CER-BDX 2023-163).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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