



Sotrovimab in SARS-COV-2 chronic hemodialysis patients in the Omicron era. Is intradialytic administration feasible? Report of 4 cases

Emanuele Mambelli¹ · Lorenzo Gasperoni¹ · Laura Maldini¹ · Carlo Biagetti² · Angelo Rigotti¹

Received: 1 May 2022 / Accepted: 21 August 2022

© The Author(s) under exclusive licence to Italian Society of Nephrology 2022

Abstract

Chronic hemodialysis patients are at high risk of morbidity and mortality in case of SARS-CoV-2 infection and they may need to be treated with monoclonal antibodies, either because they have not been vaccinated, or because they have a low anti spike antibody titer. Administration of Sotrovimab has recently been proposed for hemodialysis patients, but data are on the results lacking. We report on four cases of chronic dialysis patients who received Sotrovimab during intermittent dialysis sessions. In our series, no adverse reactions were recorded; intradialytic administration resulted safe and allowed an adequate observation time without prolonging hospital stay in chronic hemodialysis outpatients.

Keywords Sotrovimab · SARS-CoV-2 · Hemodialysis · COVID-19

Introduction

Since dialysis patients are at higher risk for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2)-related morbidity and mortality [1, 2], they have been included among the high risk categories eligible for monoclonal antibody therapy, which demonstrated a reduction of hospitalization rates and mortality [3, 4].

Sotrovimab, formerly known as VIR-7831, is an engineered human monoclonal antibody derived from the parent antibody S309 identified in 2003 SARS-CoV survivors [5].

The prespecified interim analysis of the COMET-ICE trial demonstrated the efficacy of Sotrovimab in reducing the risk of disease progression in non-hospitalized COVID-19 patients with risk factors for severe disease. Although chronic kidney disease was among the risk factors that led to Sotrovimab administration, few of these patients were enrolled and none of them was on chronic dialysis treatment [6].

Sotrovimab retained protection against the Omicron BA.1 variant of concern (VOC), but lost efficacy against the Omicron BA.2 VOC. Thus, once BA.2 spread throughout our territory, the Italian Medicines Agency (AIFA) blocked its use [7].

Alternatively, a short course of the antiviral remdesivir among non-hospitalized patients who were at high risk for Covid-19 progression demonstrated an 87% lower risk of hospitalization or death than placebo [8].

Unfortunately, patients with severe acute kidney injury and end stage kidney disease (ESKD) were excluded from remdesivir trials and although compassionate remdesivir use in dialysis patients was reported to be safe [9], its administration is not recommended in patients with eGFR less than 30 ml per minute [10].

In addition, nirmatrelvir plus ritonavir (paxlovid) demonstrated efficacy in reducing both hospitalization and mortality among non-hospitalized adults with mild-to-moderate COVID-19 who were at high risk for progression to severe COVID-19, but dialysis patients were excluded; given theoretical concerns about drug accumulation and safety, the drug is not recommended for those with eGFR < 30 ml per minute [11, 12]. Nonetheless, a small case series of 15 dialysis patients with COVID-19 treated with lower doses of nirmatrelvir/ritonavir reported rapid symptom resolution with no adverse events [13].

✉ Emanuele Mambelli
emanuele.mambelli@auslromagna.it

¹ U.O. Nefrologia e Dialisi, Ospedale Infermi, AUSL Romagna, Rimini, Italy

² U.O. Malattie Infettive, Ospedale Infermi, AUSL Romagna, Rimini, Italy

We report a case series of four SARS-CoV-2 chronic hemodialysis patients, all of whom were outpatients, who underwent intradialytic Sotrovimab administration. Infection recovery was defined as a negative nasopharyngeal swab after at least three days without symptoms.

The cases

Pt#1

A 46-year-old male with ESKD due to hypertensive nephropathy was on twice weekly hemodialysis through a proximal arteriovenous fistula. His urinary output and hemodialysis Kt/V were 1500 ml/day and 1.47, respectively. He was not vaccinated for SARS-CoV-2. Nasopharyngeal swab was performed because of fever while neither cough nor respiratory failure were present. Symptoms started on day 0 and sotrovimab 500 mg was administered on day 5 during the dialysis session. No adverse reactions were recorded. He experienced rapid clinical improvement with infection recovery after 12 days.

Pt#2

An 87-year-old male with ESKD due to hypertensive nephropathy was on twice weekly hemodialysis through a jugular tunneled central venous catheter. His hemodialysis Kt/V was 1.25 and urinary output was 1700 ml/day.

Comorbidities included chronic heart failure, pace-maker for atrio-ventricular block and hypertension. He received 3 doses of the anti-SARS-CoV-2 mRNA vaccine, and his anti spike IgG titer at diagnosis was 1410 BAU/mL. The only symptom was cough. The patient was tested on day 0 and received sotrovimab 500 mg on day 3 during the dialysis session. No adverse reactions were recorded. Symptoms gradually improved and he recovered from infection after 14 days.

Pt#3

A 92-year-old male with ESKD was on hemodialysis thrice weekly through a distal arterio venous fistula. Comorbidities included hypertension, ulcerative colitis and psoriasis. He received 3 doses of anti-SARS-CoV-2 mRNA vaccine and his antibody titer was > 2080 BAU/mL at the time of infection. He experienced mild fever and cough with no respiratory failure.

Symptoms started on day 0 and sotrovimab 500 mg was administered on day 4 during the dialysis session. No adverse reactions were recorded. Symptoms resolved quickly and he recovered from infection after 12 days.

Pt#4

A 61-year-old female with ESKD due to relapsing renal stones was on hemodialysis thrice weekly through a jugular tunneled central venous catheter.

Comorbidities included fibromyalgia and deep vein thrombosis on warfarin treatment. She was not vaccinated for SARS-CoV-2. Her symptoms were fever and cough without respiratory failure.

Symptoms started on day 0 and Sotrovimab 500 mg was administered on day 5 during the dialysis session. No adverse reactions were recorded. Symptoms gradually improved and she recovered from infection after 11 days.

Intradialytic Sotrovimab administration in Chronic Hemodialysis SARS-CoV-2 outpatients

Four adult chronic hemodialysis outpatients [median age 74 years (min 46, max 92); 1 female] tested positive for SARS-CoV-2 in the Dialysis Unit of the Infermi Hospital (Rimini, Italy). Patients were diagnosed from 6th January to 17th February 2022 by nasopharyngeal swab for SARS-CoV-2 nucleic acid, using reverse transcription polymerase chain reaction (RT-PCR). The viral load was not evaluated since it is not routinely available in our hospital. Two patients were unvaccinated. The two vaccinated patients had received two doses + a booster dose of the Spikevax (ex COVID-19 Moderna mRNA-1273) Vaccine. They had mild symptoms, the most common being fever and cough (Table 1). Anti-protein S antibody was measured soon after the diagnosis of SARS-CoV-2 infection in three of the four patients. One patient was given the indication to treatment without the need for the Anti-Spike dosage since he was unvaccinated and young.

Although the SARS-CoV-2 variant was not assessed, Omicron BA1 accounted for more than 95% of cases in our district in that period [14].

Infectious disease clinicians gave the indication to therapy. Sotrovimab 500 mg was diluted in 100 ml of physiological saline solution and administered over 30 min during the second hour of a routine, planned hemodialysis session. No treatment was given other than Sotrovimab and dialysis.

No adverse reactions were recorded. All subjects were managed as outpatients until infection recovery and none of them experienced symptom worsening or respiratory failure.

Clinical, laboratory and dialysis features are shown in Table 1. Median Charlson Comorbidity Index was 4.5 (min

Table 1 Clinical history, laboratory analysis and patient outcome

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)/sex	46/male	87/male	92/male	61/female
Dialysis vintage (months)	17	3	60	40
Charlson score	2	7	6	5
Vascular access	Proximal AVF	Tunneled CVC	Distal AVF	Tunneled CVC
Comorbidities	Hypertension	PM for AVB, CHF, Hypertension	UC, psoriasis, Hypertension	DVT in VKA, fibromyalgia
SARS-COV-2 vaccination	None	3 doses	3 doses	None
Previous SARS-COV-2 infection	None	None	Yes, 21 months before re-infection	None
Dialysis technique	HD	HD	OLHDF	HD
Dialysis membrane	Polysulfone	Polysulfone	Polysulfone	Polysulfone
Dialysis schedule	Twice weekly	Twice weekly	Thrice weekly	Thrice weekly
Dialysis sessions performed during infection period (n.)	4	5	5	5
Days between symptoms onset and sotrovimab administration	5	3	4	5
Qb, mL/min, median (min;max)	300 (250;300)	300 (250;300)	300 (250;300)	280 (280;300)
Convective volume L, median (min–max)	NA	NA	14 (14;18)	NA
Fluid removal per session L, median (min–max)	1.6 (0.7 – 2)	2.3 (1.6;3.3)	2.0 (1.1;2.2)	1.5 (1.3;3.4)
Clinical and laboratory parameters at diagnosis				
Blood pressure (mmHg)	140/85	139/88	114/53	120/66
Symptoms	Fever	Cough	Mild fever and mild cough	Fever and cough
SpO2%, room air	99	98	97	98
CRP (mg/l)	13.00	17.30	14.00	42.00
LDH U/L	263	234	186	230
Anti Spike IgG BAU/ml	NA	1410	> 2080	23.6
Infection duration (days)	12	14	12	11
Follow-up (days)	42	31	30	44
Outcome	Infection recovery	Infection recovery	Infection recovery	Infection recovery

OLHDF online hemodiafiltration, HD hemodialysis, AVF arteriovenous fistula, PM pace maker, CVC central venous catheter, UC ulcerative colitis, DVT deep vein thrombosis, VKA vitamin K antagonist, CRP C-Reactive Protein

2, max 7). The median time between symptom onset and Sotrovimab administration was 4.5 days (min 3; max 5). All patients recovered from infection and symptoms.

Discussion

To our knowledge this is the first report of intradialytic Sotrovimab administration in non-hospitalized chronic hemodialysis patients.

Sotrovimab is a large protein (human immunoglobulin IgG1-kappa) with a molecular weight of 149 KDa, so it is not expected to be dialyzed.

We administered the drug during the second hour of the hemodialysis session in all four outpatients.

Intra-dialysis drug administration provided several advantages. First, it allowed an adequate length of clinical observation during the Dialysis Center stay as described for intradialytic Bamlanivimab/Etesevimab administration [15]. Sotrovimab indeed requires a single intravenous infusion over 30 min and patients should be monitored during administration, and for at least 1 h afterwards. Drug administration during the second hour of the dialysis treatment allowed us to monitor the patients until the end of the dialysis treatment itself. Furthermore, intradialytic administration avoided a further hospital access, thereby limiting the patients' discomfort.

Second, we avoided the need for patient hospitalization, thus reducing bed occupancy. Third, we avoided having to make an additional trip to the hospital and in so doing, we reduced (a) the risk of infection diffusion, (b) the use of

dedicated transport personnel and means, and (c) the consumption of personal protective equipment, therefore allowing us to decrease the utilization of resources and to lower costs.

The chronic hemodialysis outpatients described above had good outcomes. During Sotrovimab administration they had no clinical complications.

Unfortunately, we have no data concerning the viral load decline. One patient was not tested for anti-spike IgG protein before treatment. According to our Hospital protocol, follow up was performed by nasal swab and we have no data on nasopharyngeal CRP. Data regarding infection and follow up duration are shown in Table 1.

Besides the low number of patients, our experience has another limitation. Hypotension is a complication of dialysis treatment but during Sotrovimab administration it can be both dialysis-dependent and an adverse drug event. Medical history and patients' usual clinical behavior during dialysis treatment could help to interpret the event. On the other hand, drug administration during dialysis treatment has the advantage of constant monitoring and the possibility of prompt intervention.

Conclusions

In our experience, the administration of Sotrovimab during the intermittent hemodialysis session was well tolerated and no adverse reactions were observed. Intradialytic use allowed adequate observation time without prolonging hospital stay in chronic hemodialysis outpatients.

Our experience suggests that administration of Sotrovimab during dialysis is feasible.

Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

- Williamson EJ, Walker AJ, Bhaskaran K et al (2020) Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 584:430–436. <https://doi.org/10.1038/s41586-020-2521-4>
- Goffin E, Candellier A, Vart P et al (2021) COVID-19-related mortality in kidney transplant and haemodialysis patients: a comparative, prospective registry-based study. *Nephrol Dial Transplant* 36:2094–2105. <https://doi.org/10.1093/ndt/gfab200>
- Chen P, Nirula A, Heller B et al (2021) SARS-CoV-2 neutralizing antibody LY-CoV555 in outpatients with COVID-19. *N Engl J Med* 384:229–237. <https://doi.org/10.1056/NEJMoa2029849>
- Weinreich DM, Sivapalasingam S, Norton T et al (2021) REGN-COV2, a neutralizing antibody cocktail, in outpatients with COVID-19. *N Engl J Med* 384:238–251. <https://doi.org/10.1056/NEJMoa2035002>
- Pinto D, Park Y-J, Beltramello M et al (2020) Cross-neutralization of SARS-CoV-2 by a human monoclonal SARS-CoV antibody. *Nature* 583:290–295. <https://doi.org/10.1038/s41586-020-2349-y>
- Gupta A, Gonzalez-Rojas Y, Juarez E et al (2021) Early treatment for COVID-19 with SARS-CoV-2 neutralizing antibody Sotrovimab. *N Engl J Med* 385:1941–1950. <https://doi.org/10.1056/NEJMoa2107934>
- Iketani S, Liu L, Guo Y et al (2022) Antibody evasion properties of SARS-CoV-2 Omicron Sublineages. *Nature* 604:553–556. <https://doi.org/10.1038/s41586-022-04594-4>
- Gottlieb RL, Vaca CE, Paredes R et al (2022) Early Remdesivir to prevent progression to severe COVID-19 in outpatients. *N Engl J Med* 386:305–315. <https://doi.org/10.1056/NEJMoa2116846>
- Aiswarya D, Arumugam V, Dineshkumar T et al (2021) Use of Remdesivir in patients With COVID-19 on hemodialysis: a study of safety and tolerance. *Kidney Int Rep* 6:586–593. <https://doi.org/10.1016/j.ekir.2020.12.003>
- Adamsick ML, Gandhi RG, Bidell MR et al (2020) Remdesivir in patients with acute or chronic kidney disease and COVID-19. *J Am Soc Nephrol* 31:1384–1386. <https://doi.org/10.1681/ASN.2020050589>
- Hammond J, Leister-Tebbe H, Gardner A et al (2022) Oral Nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. *N Engl J Med* 386:1397–1408. <https://doi.org/10.1056/NEJMoa2118542>
- Hiremath S, McGuinty M, Argyropoulos C et al (2022) Prescribing Nirmatrelvir/Ritonavir (Paxlovid) for COVID-19 in advanced chronic kidney disease. *Clin J Am Soc Nephrol CJN*. <https://doi.org/10.2215/CJN.05270522>
- Brown PA, McGuinty M, Argyropoulos C et al (2022) Early experience with modified dose nirmatrelvir/ritonavir in dialysis patients with coronavirus disease-2019. *Nephrology* 399(10334):1513
- <http://rr.auslromagna.it/comunicazione/emergenza-covid-19/documenti-covid/epidemiologia/bollettino-covid-19>
- Gasparoni L, Abenavoli C, Donati G et al (2022) Safety of Intradialytic Bamlanivimab/Etesevimab administration in two COVID-19 dialysis outpatients. *Blood Purif*. <https://doi.org/10.1159/000521637>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.