Clinical Impact, Reactogenicity, and Immunogenicity After the First CoronaVac Dose in Kidney Transplant Recipients

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In phase 3 trial, inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine (CoronaVac, Sinovac Life Sciences, Beijing, China) was associated with 71.1% seroconversion at least 14 d after the second dose, showing 50.7% efficacy against symptomatic COVID-19 among healthcare workers.[1] Currently, this vaccine has been approved for emergency use in 24 countries, including Brazil, where the national vaccination program was launched on January 1, 2021, following the age criterion.

Kidney transplant recipients have shown 20%–30% COVID-19-associated fatality rates,[2] have been excluded in vaccine trials, and had no early priority for vaccination. Therefore, this single-center, prospective, 12-mo follow-up study was designed to assess clinical impact, reactogenicity, and immunogenicity of CoronaVac.

Between March 20 and 28, 2021, 3354 patients aged 30–69 y, >30 d of transplantation, and no previous COVID-19 received standard 2-dose schedule of CoronaVac (3 μg each dose, 28 d apart). Patients were scheduled to receive the vaccine on 2 consecutive weekends, with approximately 800–900 patients per d, from 7 AM to 7 PM All communication resources were used to reach them within 3 wk before the vaccination day (telephone call, SMS text messages, WhatsApp messages). Workstations were set up at the outpatient clinic and patients were admitted in groups of 30 persons to (1) obtain general information regarding COVID-19, the clinical study, the vaccine, and preventive measures; (2) inform consent discussion and signature; (3) registration of the patient in the electronic medical records of the institution; (4) blood sampling for serology followed by vaccination, and a reminder of the scheduled second dose. All employees of the institution were invited to participate in the vaccination campaign, and >300 professionals volunteered for the activity, including students from different universities.

The study was approved by the local ethics committee, registered at ClinicalTrials.gov, NCT04801667, and all patients signed an informed consent form. At day 28, a prespecified questionnaire was obtained to capture adverse reactions to the vaccine or newly diagnosed SARS-CoV-2 infection. Sample size for the immunogenicity cohort (942 patients seronegative for immunoglobulin [Ig]G anti-SARS-CoV-2 before the first dose) was calculated using the age distribution and seroconversion rate (71%) of the phase 3 study,[1] with 95% confidence interval and an absolute error of 10%. Antibody response at day 28 was assessed using the AdviseDx SARS-CoV-2 IgG II assay (Abbot Laboratories, IL). Values >50 AU/mL were considered positive.[3]

Characteristics and outcomes of the study population (n = 3354) are in Table 1. The patients were predominantly male, median age of 52 (interquartile range [IQR], 44–60) y, low prevalence of diabetes mellitus, and median time posttransplant of 7 (IQR, 3–12) y. Seroprevalence of IgG anti-SARS-CoV-2 nucleocapsid protein at D0 was 3.6%, and these seropositive patients at the time of vaccine were excluded for the analysis of the antibody responses. Among the seronegative patients at D0, there were 1012 individuals randomly selected for the immunogenicity analysis. The other patients did not have any testing performed after the vaccination. After the first vaccine dose, 61 (1.8%) patients had COVID-19 confirmed by reverse transcription-polymerase chain reaction or antigen test at a median time of 12 (IQR, 8–16) d. Of them, 44 (72%) required hospitalization and 16 (26%) died 14–49 d after the first vaccine dose.

The most common adverse reaction was local pain/tenderness (11%). Systemic symptoms occurred in 5% or less of the patients; no severe adverse reaction was observed. There was only 1 episode of acute cellular rejection (Banff IB) 6 d after vaccination in a patient with documented nonadherence that showed partial recovery of renal function after treatment with methylprednisone and antithymocyte globulin.

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TABLE 1.

Baseline demographic characteristics, outcomes, adverse reactions, and immunogenicity of the first dose of CoronaVac in kidney transplant recipients

Parameters	Overall (N = 3354)	Immunogenicity cohort (n = 942)	*P*	IgG (+) D28 (n = 143)	IgG (–) D28 (n = 799)	*P*
Demographic characteristics						
Median age, (IQR), y	52 (44–60)	50 (43–56)	<0.001	47 (41–54)	51 (43–57)	<0.001
30–60 y, n (%)	2552 (76)	844 (90)		136 (95)	708 (89)	
>60 y, n (%)	802 (24)	98 (10)		7 (5)	91 (11)	
Male gender, n (%)	2008 (60)	544 (58)	0.269	76 (53)	468 (59)	0.556
Diabetes mellitus, n (%)	333 (10)	93 (10)	>0.99	10 (7)	83 (10)	0.208
Organ, n (%)						
Kidney	3239 (96)	835 (89)	<0.001	140 (98)	695 (87)	<0.001
Simultaneous pancreas-kidney	115 (4)	107 (11)		3 (2)	104 (13)	
Median length of transplant, (IQR), y	7 (3–12)	6 (3–11)	<0.001	6 (3–11)	6 (3–11)	>0.99
Maintenance immunosuppressive regimen, n (%)						
TAC-Pred-AZA	1002 (30)	282 (30)	0.231	34 (24)	248 (31)	0.253
TAC-Pred-MPA	1396 (42)	402 (43)		66 (46)	336 (42)	
CSA-Pred-AZA	376 (11)	89 (9)		11 (8)	78 (10)	
TAC-Pred-mTORi	306 (9)	102 (11)		18 (12)	84 (10)	
Other	274 (8)	67 (7)		14 (10)	53 (7)	
Outcomes						
COVID-19 diagnosis after the first dose, n (%)	61 (1.8)					
Median age, (IQR), y	53 (47–59)					
Time from first dose to COVID-19 (d), n (%)						
≤7	13 (21)					
8–14	23 (38)					
>14	25 (41)					
Need for hospitalization, n (%)	44 (72)					
Need for intensive care, n (%)	27 (44)					
Lethality from COVID-19, n (%)	16 (26)					
Adverse reactions to the vaccine, n (%) (n = 3274)						
Local pain or tenderness	378 (11)					
Headache	178 (5)					
Myalgia	160 (5)					
Runny nose	113 (3)					
Diarrhea	93 (3)					
Sore throat	65 (2)					
Fever	39 (1)					
Serologic status before vaccination, n (%)						
Negative	3182 (95)	942		—	—	
Positive	122 (4)	0		—	—	
Indeterminate	50 (1)	0		—	—	
Serologic status after the first dose, n (%)						
Negative (<50 AU/mL)	—	799 (85)				
Positive[a]	—	143 (15); 95% CI, 13%-17%				
30–60 y, n (%)		134 (16); 95% CI, 14%-19%				
>60 y, n (%)		9 (8); 95% CI, 3%-13%				

[a]*P* = 0.026 for comparison between the 2 age ranges.

AZA, azathioprine; CI, confidence interval; COVID-19, coronavirus disease 2019; CSA, cyclosporine; IgG, immunoglobulin G; IQR, interquartile range; MPA, mycophenolate; mTORi, mammalian target of rapamycin inhibitors; Pred, prednisone; TAC, tacrolimus.

Seroconversion 28 d after the first dose was 15.2% (95% confidence interval, 12.9%-17.5%), with median IgG value of 477 AU/mL (IQR, 123–1705). Patients aged >60 y or those who underwent combined kidney-pancreas transplants had lower seroconversion than those aged <60 y and underwent isolated kidney transplants.

The potential advantage of the traditional inactivated vaccines, the induction of a broader polyclonal immune response,[4] was not associated with a higher seroconversion rate compared with the newer RNA-based COVID-19 vaccines.[5] In this ongoing prospective study, there was no obvious clinical impact after the first dose, as

demonstrated by the 26% lethality rate, similar to that of unvaccinated kidney transplant recipients.[2] CoronaVac vaccine was safe, but seroconversion after the first dose was low, similar to what was reported to the RNA-based vaccines. The elderly showed even lower rates of seroconversion. These findings support the need for maintaining individual protection measures, even after the first dose of the vaccine.

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