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CLINICAL STUDY

Immunogenicity and safety of the CoronaVac vaccine in patients undergoing treatment for breast and lung cancer

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ABSTRACT

BACKGROUND: Patients with cancer receiving an active systemic therapy are at a high risk for coronavirus disease (COVID-19); however, the antibody response and long-term results of the inactivated whole-virion SARS-CoV-2 (CoronaVac) vaccine in these patients compared to the non-cancer population are unknown.

OBJECTIVE: To compare seroconversion for SARS-CoV-2 receptor-binding domain (RBD) specific IgG positivity against two doses of the CoronaVac vaccine in breast and lung cancer patients receiving systemic therapy, to determine the factors affecting seropositivity, and to observe long-term results up to a secondary booster vaccine.

RESULTS: The analysis included 201 cancer patients (99 breasts, 102 lungs; median age: 59 years (range: 28–92), 42.3 % men) and 97 controls (median age: 62 years (range: 24–87), 38.1 % men). The seropositivity rate for RBD IgG after 2 doses of vaccine in the cancer group was 81.6 % (n=164) and 93.8 % (n=91) in the control group (p=0.005). The median IgG titer of cancer patients was significantly lower than in the control group (338 (IQR, 95–933) AU/mL vs 676 (IQR, 389–1270) AU/mL; p<0.001). Multivariate analysis of all the patients determined that having cancer (OR: 0.303, 95%CI: 0.123–0.750, p=0.010) and being over 60 years of age (OR: 0.447, 95%CI: 0.218–0.917, p=0.028) was associated with a reduced vaccine response. A subgroup analysis of cancer patients revealed that seroconversion was lower in men than in women (75.3 % vs 86.2 %, p=0.049) and lower in ≥60 patients than in <60 patients (75.9 % vs 89.4 %, p=0.014).

DISCUSSION AND CONCLUSION: Cancer patients receiving an active systemic therapy with two doses of the CoronaVac vaccine had a lower antibody response than the non-cancer population, and deaths due to COVID-19 may occur in these patients despite the vaccine. Therefore, extensive protective measures should be taken to protect against COVID-19 in cancer patients aged 60 years and older, who have received two doses of the CoronaVac vaccine *(Tab. 4, Fig. 4, Ref. 27)*. Text in PDF *www.elis.sk*

KEY WORDS: vaccine, coronavac, cancer, covid-19, sars-cov-2.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global problem with a high morbidity and mortality (1). While vaccine studies continue, social distancing, face masks, and individual contact isolation precautions have been the primary strategy to break the chain of transmission and prevent a collapse in healthcare systems. After completing the phase 3 study of the mRNA COVID-19 vaccine with 43,548 participants, it was approved as the first COVID-19 vaccine in the UK on December 2, 2020 (2), and the vaccination period of the pandemic began. CoronaVac (Sinovac Life Sciences, Beijing, China), one of the coronavirus vaccines, is an inactivated whole-virion SARS-CoV-2 vaccine, which neutralizes ten representative strains of SARS-Cov-2, has a high efficacy against PCR-confirmed symptomatic COVID-19 with a good tolerance and safety profile (3, 4). In the first months of 2021, healthcare workers and high-risk individuals started to be vaccinated with the inactivated CoronaVac in countries such as Turkey and Chile (5, 6). It has been approved for use in 41 countries in October 2021 and has a widespread use (7).

Whether they receive chemotherapy or not, cancer patients are at increased risk for COVID-19 than the overall population (8). Although some of the first published data support this hypothesis,

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it has later been reported that cancer patients are at equal risk with the non-cancer population. The higher COVID-19-associated mortality rate in cancer patients is due to risk factors such as having lung cancer, advanced age, and comorbidities (9, 10, 11, 12, 13). Regardless of the cause, delays in cancer treatment (e.g., systemic anticancer treatment, cancer surgery, radiotherapy treatment) are associated with a worse survival (14, 15). For such reasons, many organizations, including the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO), recommend an immediate vaccination for patients receiving an active chemotherapy (16, 17, 18).

Influenza vaccine studies published in previous years have shown that inactive influenza vaccines develop less immunogenicity in the patients receiving an active immunosuppressive therapy than in healthy people (19, 20). The patients receiving immunosuppressive therapy were not included in the inactivated COVID-19 vaccine studies. Therefore, the efficacy and safety of the CoronaVac vaccine in cancer patients receiving systemic treatment are unknown (21, 22). A single-arm, 47-patient study, one of the first studies with CoronaVac, determined approximately 59.5 % antibody response in cancer patients receiving systemic chemotherapy (23).

This multicenter, non-randomized, prospective, observational study compares the efficacy of the CoronaVac vaccine in breast and lung cancer patients receiving the active systemic therapy (cytotoxic chemotherapy, monoclonal antibody) with that of non-cancer volunteers.

Materials and methods

Study design and participants

This non-randomized, controlled, and open-label study was conducted in 3 cancer centers in Turkey between March 3, 2021, and October 21, 2021. All the participants were informed about the study, and their written consent was obtained. The study was conducted under the Declaration of Helsinki, Good Clinical Practice guidelines of the International Council for Harmonization. Necessary approvals were obtained from Tekirdag Namik Kemal University, Clinical Research Ethics Committee (2021.01.02.01), and Turkey Medicines and Medical Devices Agency (E-61749811-514.05.01-394423). This study was registered on clinicaltrials.gov under NCT04765215.

Participants aged 18 years and over, who had not been infected with SARS-CoV-2 before, were evaluated in 2 groups. The cancer group consisted of patients with breast or lung cancer, who received two doses of CoronaVac vaccine during the active systemic therapy (cytotoxic chemotherapy, monoclonal antibody), with an Eastern Cooperative Oncology Group performance status of 0–2, a life expectancy of more than 12 weeks, and at least six weeks of chemotherapy after the first vaccination. The control group consisted of relatives of cancer patients without an immunosuppressive disease, healthcare workers, and volunteers that applied to the internal medicine outpatient clinic, who received two doses of the CoronaVac vaccine. The participants with a previous COVID-19 infection or suspected close contact or an immunosuppressive disease (i.e., solid organ transplant, HIV infection) were excluded from the study. All the patients were vaccinated under the vaccination program of the Ministry of Health (Fig. 1).

Outcomes

The study's primary endpoint was the antibody response induced by the CoronaVac vaccine in the cancer patients receiving the systemic therapy compared to the non-cancer control group. The secondary endpoint was the long-term follow-up data of the groups on COVID-19 infection from the 2nd dose of vaccination to the booster dose or until the date of exitus.

Procedures

CoronaVac is the vaccine containing 3 µg of inactivated SARS-CoV-2 virus and some auxiliary substances (aluminum hydroxide, disodium hydrogen phosphate, monosodium hydrogen phosphate, sodium hydroxide, etc.) in each 0.5 ml dose. It is administered intramuscularly according to the dosing schedule of day 0 and day 28. Since the study was not invasive, the planned systemic treatment dates and the time between the systemic treatment of the patients and the vaccination were left to the patient's preference without any intervention.

Side effects were recorded separately after the first dose and the second dose. Blood samples for antibody measurement were collected between 21–35 days after the second dose of the CoronaVac vaccine. Blood samples of the cancer patients were taken on the day of treatment before receiving their antineoplastic therapy. The blood samples were centrifuged and stored at -80 ºC till reaching the target number of the patients, and then SARS-CoV-2

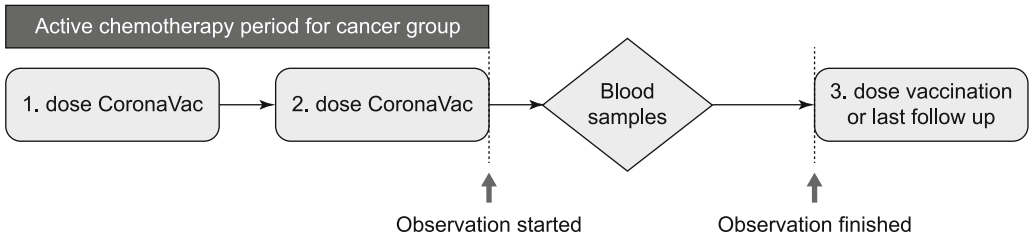

Fig. 1. Study design.

Tab. 1. Patient characteristics.

	Patients with cancer (n=201)	Control (n=97)	p
Median age. Years (min–max)	62 (24–87)	59 (28–92)	0.295
Sex			
male	85 (42.3%)	37 (38.1%)	0.495
female	116 (57.7%)	60 (61.9%)	
Cardiovascular disease*			
yes	59 (29.4%)	36 (37.1%)	0.178
no	142 (70.6%)	61 (62.9%)	
Diabetes mellitus			
yes	38 (18.9%)	24 (24.7%)	0.245
no	163 (81.1%)	73 (75.3%)	
Chronic respiratory disease			
yes	38 (18.9%)	13 (13.4%)	0.237
no	163 (81.1%)	84 (86.6%)	
Cancer Type			
breast	99 (49.3%)	0	N/A
lung	102 (50.7%)	0	

*Cardiovascular diseases – ischemic heart disease, hypertension, hypercholesteremia. N/A – Not applicable

receptor-binding domain (RBD) specific IgG levels were quantitatively measured by ELISA.

Interpretation of antibody test results and evaluation of immunogenicity

Anti-SARS-CoV-2 IgG antibody levels in the participants' blood were measured using the SARS-CoV-2 IgG II Quant kit (Abbott, Ireland) on the Abbott Alinity device. This test evaluates the immune status of individuals by measuring immunoglobulin class G (IgG) antibodies against the receptor-binding domain (RBD) of the S1 subunit of the spike protein of SARS-CoV-2. Results are reported as relative light units (RLU). The test has been compared with the neutralization test and the immunofluorescence assay and has shown a very high specificity (24, 25).

The manufacturer's Cutoff value of the IgG test is 50.0 AU/ml. Measurement results were interpreted as negative if < 50.0 AU/ml and positive if ≥ 50.0 AU/ml and defined as seroconversion.

Sample size

The phase I/II study with Coronovac reported 99.2 % seroconversion on day 28 in the group given 3 µg vaccine (21). The sample size calculation using MedCalc (MedCalc software Ltd, Acacialaan, 22 8400 Ostend, Belgium), taking $pH_0 = 99.2$ %, $pH_1 = 90.2$ %, determined that a sample of 194 people (97 studies, 97 controls) was sufficient to compare the two groups with 80 % power and 5 % alpha error using Chi-square analysis. However, to compare the breast and lung cancer patients in the cancer group with the control group as a subgroup analysis, a total of 291 patients, 97 breast cancer, 97 lung cancer, and 97 control group, were planned to be included in the study.

Statistical analysis

The results were presented as numbers, percentage, median (minimum-maximum), mean and standard deviation. Chi-square (Fisher's exact test when necessary) was used for the categorical comparison of the groups; Spearman correlation analysis was used to assess the correlation between antibody levels and age, and the Man–Whitney U test was used for the comparison of the groups' qualitatively measured antibody levels. Factors affecting RBD positivity (≥ 50.0 AU/ml) were investigated using a binary logistic regression model constructed in univariate and multivariate analyses. Cases with the p of less than 0.05 and a Type 1 error of 5 % were considered statistically significant. All the statistical analyses were performed using the SPSS 24 (SPSS Inc., Chicago, III) software.

Results

This study included cancer patients, who received two doses of the CoronaVac vaccine during active chemotherapy between January 14, 2021, and July 1, 2021. Blood samples were taken at the mean of 27.9 ± 3.1 days after the second dose of vaccine, just before the intravenous systemic treatment. Volunteers without a history of immunosuppressive disease or cancer were included in the study as a control group. Their serum samples were taken for antibody measurement, on average 28.2 ± 3.2 days after the second dose of CoronaVac. A total of 304 serum tests were analyzed, but after excluding six samples (5 cancers – 1 control) due to not being collected in the appropriate time interval, 298 participants were included in the study.

Tab. 2. Comparison of post-vaccine SARS-COV-2 Receptor-binding domain (RBD) specific IgG positivity in the cancer patients who received two doses of CoronaVac during active chemotherapy and the control group.

	Patients with cancer (n=201)	Control group (n=97)	p
RBD-IgG < 50.0 AU/mL (negative)	n=37 (18.4%)	n=6 (6.2%)	0.005
RBD-IgG ≥ 50.0 AU/mL (positive)	n=164 (81.6%)	n=91 (93.8%)	

Tab. 3. Analysis of factors affecting SARS-COV-2 Receptor-binding domain (RBD) specific IgG positivity in all the patients (n = 298).

Variable	Category	Univariate analysis		Multivariate analysis	
		OR (95% CI)	p	OR (95% CI)	p
Study population	no cancer/cancer	0.292 (0.119–0.719)	0.007	0.303 (0.123–0.750)	0.010
Age	18–59/≥60	0.429 (0.211–0.872)	0.019	0.447 (0.218–0.917)	0.028
Sex	Male / Female	2.024 (1.054–3.887)	0.034		
CVD	No/Yes	0.674 (0.346–1.313)	0.246		
DM	No/Yes	0.549 (0.267–1.129)	0.103		
CRD	No/Yes	0.541(0.252–1.162)	0.115		

CVD – cardiovascular disease, DM – diabetes mellitus, lung disease-chronic, CRD – chronic respiratory disease

Patient characteristics

The study included 201 cancer patients (99 breast cancer, 102 lung cancer) and 97 volunteers as a control group. The median age of cancer patients was 59 years (min:

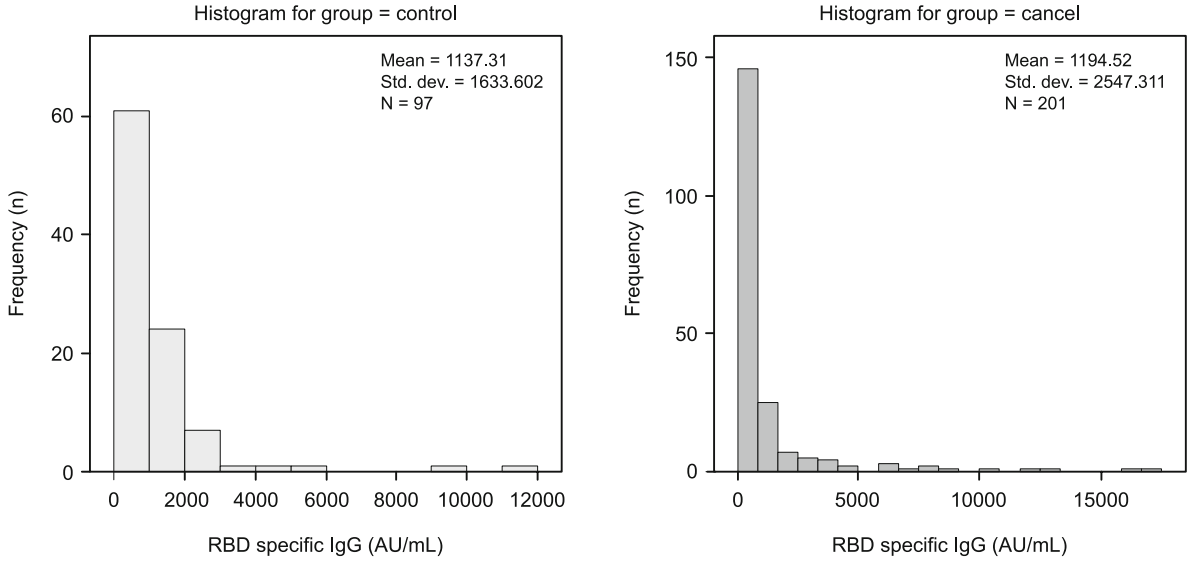

Fig. 2. Distribution of SARS-COV-2 Receptor-binding domain (RBD) specific IgG levels by groups.

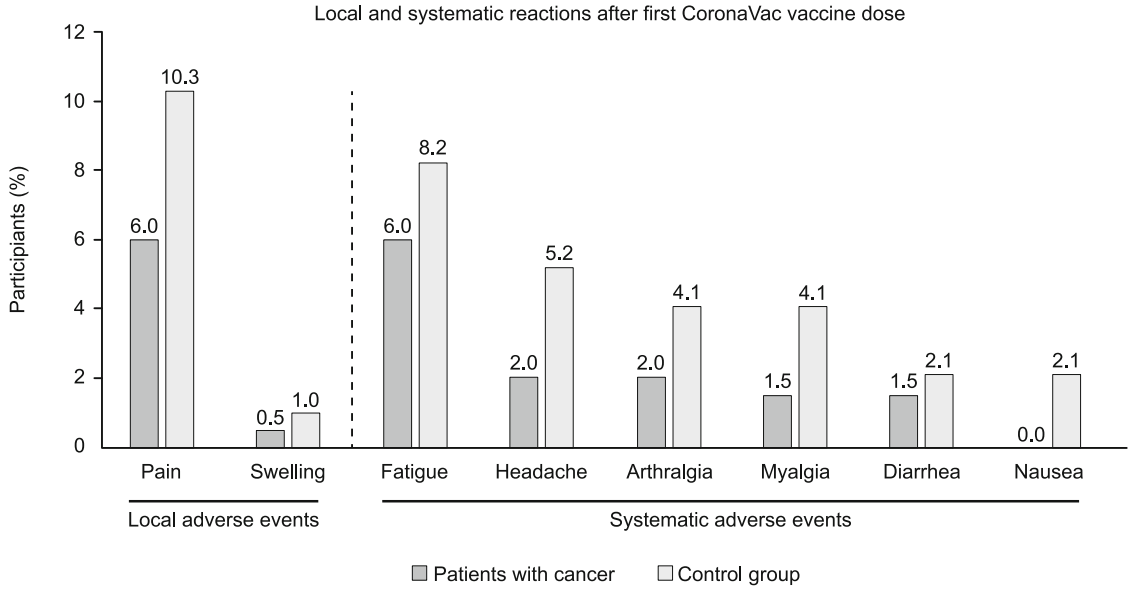

Fig. 3. Adverse events observed after the first dose of CoronaVac vaccine.

28 – max: 92), and the median age of the control group was 62 years (min: 24 – max: 87). The ages of the 2 groups were statistically similar (p = 0.295). There was no difference between the groups in terms of cardiovascular disease (p = 0.495), diabetes mellitus (p = 0.245), and chronic obstructive pulmonary disease (p = 0.237) (Tab. 1).

Immunogenicity after 2 doses of CoronaVac vaccination

SARS-CoV-2 receptor-binding domain (RBD) specific IgG response was measured from blood samples obtained at the mean of 28±3.1 days (cancer: 27.9±3.1, control: 28.2±3.2, p=0.142) after two doses of vaccination. Of the patients receiving an active chemotherapy, 81.6 % (n=164) were RBD IgG positive and 18.4 % (n=37) were RBD IgG negative. In the control group, RBD IgG was positive in 93.8 % (n=91) participants and negative in 6.2 % (n=6) participants (p=0.005) (Tab. 2).

The median RBD IgG level was 338 (IQR, 95–933) AU/mL in cancer patients and 676 AU/mL (IQR, 389–1270) in the control group (p<0.001) (Fig. 2). There was a weak negative correlation between the age and antibody level in cancer patients (r = –0.352, p0.001), but no correlation in the control group (r = –0.088, p=0.393).

Antibody positivity in all the participants was evaluated by univariate logistic regression analysis. RBD IgG positivity was approximately 3-fold lower in the cancer patients than in the control group (OR: 0.292, 95%CI: 0.119–0.719, p=0.007). RBD IgG positivity was lower in the participants aged 60 years and older than < 60 years (OR: 0.429, 95%CI: 0.211–0.872, p=0.019) and about 2-fold higher in women than in men (OR: 2.024, 95%CI: 1.054–3.887, p=0.034).

In multivariate analysis, being a cancer patient with two doses of CoronaVac vaccine during active chemotherapy (OR: 0.303, 95%CI: 0.123–0.750, p=0.010) and being over 60 years old (OR: 0.447, 95%CI: 0.218–0.917, p=0.028) established a negative predictive model for RBD IgG positivity (Tab. 3).

Comparison of RBD-specific IgG positivity according to demographic and clinical characteristics of cancer patients is shown in the Table 4. In the multivariate analysis of cancer patients, only 60 years of age or older formed a predictive model for seroconversion (OR: 0.372, 95%CI: 0.165–0.838, p=0.017).

Tab. 4. Univariate analysis of the factors affecting receptor-binding domain (RBD) specific IgG positivity in the cancer patients receiving active systemic therapy.

	Total	RBD-IgG <50.0 AU/mL (negative) (n=37)	RBD-IgG ≥50.0 AU/mL (positive) (n=164)	p
Sex				
• Male	85	21 (24.7%)	64 (75.3%)	0.049
• Female	116	16 (13.8%)	100 (86.2%)	
Age				
• <60	85	9 (10.6%)	76 (89.4%)	0.014
• ≥60	116	28 (24.1%)	88 (75.9%)	
Primary malignancy				
• Lung Cancer	102	23 (22.5%)	79 (77.5%)	0.124
• Breast Cancer	99	14 (14.1%)	85 (85.9%)	
Treatment modality, n (%)				
• Adjuvant or Neoadjuvant	102	23 (22.5%)	79 (77.5%)	0.124
• Palliative	99	14 (14.1%)	85 (85.9%)	
Prophylactic G-CSF	0			
• no	79	17 (21.5%)	62 (78.5%)	0.360
• yes	122	20 (16.4%)	102 (83.6%)	
Cardiovascular disease				
• no	142	22 (15.5%)	120 (84.5%)	0.098
• yes	59	15 (25.4%)	44 (74.6%)	
Diabetes mellitus				
• no	163	26 (16.0%)	137 (84.0%)	0.063
• yes	38	11 (28.9%)	27 (71.1%)	
Chronic respiratory disease				
• No	163	28 (17.2%)	135 (82.8%)	0.351
• yes	38	9 (23.7%)	29 (76.3%)	
Treatment Regimens, n (%)				
• Trastuzumab Emtansine	12	1 (8.3%)	11 (91.7%)	
• Cyclophosphamide/epirubicin	12	0 (0.0%)	12 (100.0%)	
• Carboplatin/paclitaxel	30	10 (33.3%)	20 (66.7%)	
• Docetaxel	8	0 (0.0%)	8 (100.0%)	
• Gemcitabine	7	2 (28.6%)	5 (71.4%)	
• Docetaxel and trastuzumab and/or pertuzumab	13	2 (15.4%)	11 (84.6%)	
• Trastuzumab and/or pertuzumab	18	1 (5.6%)	17 (94.4%)	N/A
• Trastuzumab/paclitaxel	8	2 (25.0%)	6 (75.0%)	
• Paclitaxel (weekly)	32	9 (28.1%)	23 (71.9%)	
• Pemetrexed	14	2 (14.3%)	12 (85.7%)	
• Cisplatin/etoposide	5	0 (0.0%)	5 (100.0%)	
• Cisplatin/gemcitabine	13	3 (23.1%)	10 (76.9%)	
• treatment switch	9	2 (22.2%)	7 (77.8%)	
• other	20	3 (15.0%)	17 (85.0%)	

G-CSF – Granulocyte colony-stimulating factor, N/A – Not applicable

Adverse events

None of the participants had Grade 3 (Severe) and Grade 4 (Potentially Life-threatening) adverse events. The most common side effects observed after the first dose of vaccine in the cancer patients and the control group were arm pain (6.0 % vs 10.3 %, respectively), fatigue (6.0 % vs 8.2 %), and headache (2 % vs 5.2 %). After the second dose, the most common side effects were fatigue (5.5 %) in the cancer patients and arm pain in the control group (10.3 %) (Figs 3 and 4).

Effectiveness of 2 doses of CoronaVac in COVID-19 prevention

The non-boost period or time to death was determined from the national digital health system (e-pulse), hospital records, and oncology follow-ups as the median of 124 days in the cancer patients (IQR, 98–156) and 129 days in the control group (IQR, 100–158). Three patients were infected with polymerase chain reaction (PCR) positive active SARS-COV-2 infection in the cancer group. Of these patients, two lung cancer patients died due to COVID-19 pneumonia. One breast cancer patient was SARS-COV-2 PCR positive on day 87 after the second dose of CoronaVac, and her systemic chemotherapy was continued after home quarantine.

Case 1

An 85-year-old male patient with chronic obstructive pulmonary disease, chronic heart disease, and benign prostatic hypertrophy. He was using 50 mg of metoprolol, 100 mg of acetylsalicylic acid, 10 mg of alfuzosin, and long-acting beta-agonists, plus inhaled corticosteroids daily. In January 2021, weekly chemotherapy of carboplatin (2 auc) and paclitaxel (80 mg/m^2) was started for bone metastatic, non-small cell lung cancer (adenocarcinoma). He received two doses of the CoronaVac vaccine on February 11, 2021, and March 14, 2021. The RBD IgG level measured 24 days after the second dose of the vaccine was 11.2 AU/mL (negative). Approximately one month after the second dose of CoronaVac vaccine, the patient who applied to the emergency department with complaints of abdominal pain and diarrhea had creatine 1.93 mg/dl, hemoglobin 6.69 g/dl, neutrophil 140/mm^3, platelet 87.000/µL. His SARS-COV-2 PCR test was positive. Filgrastim 30 MIU0.5

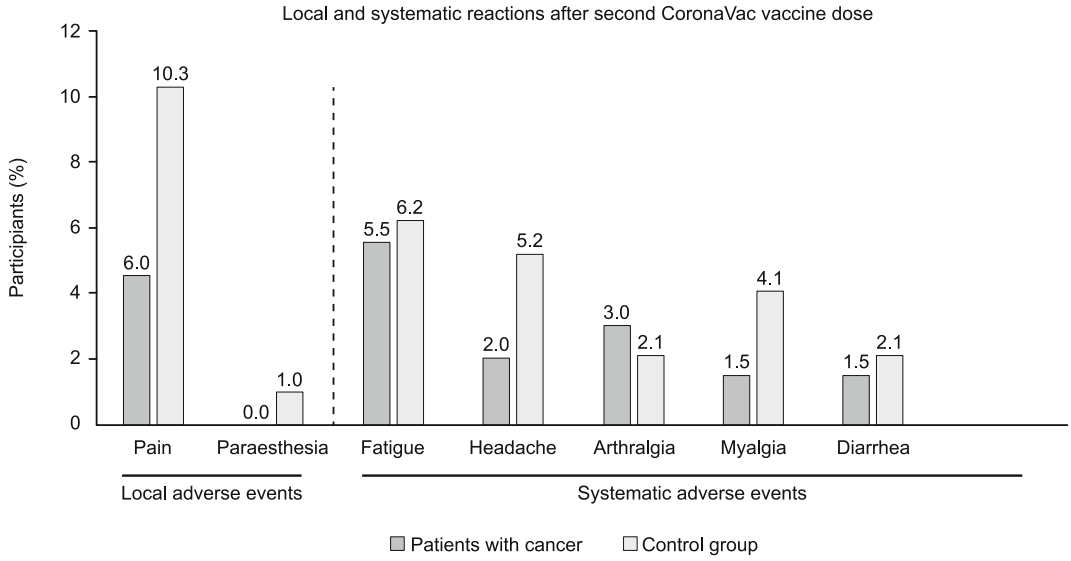

Fig. 4. Adverse events observed after the second dose of CoronaVac vaccine.

ML, piperacillin-tazobactam 9 g/day, favipiravir 3.2 g loading, 1.2 g maintenance were started as a treatment for infection, and supportive treatment was given. Upon developing respiratory failure on day 10 of his hospitalization, he was connected to an invasive mechanical ventilator and died with cardiac arrest on day 15.

Case 2

A 72-year-old male patient with arterial hypertension, coronary artery disease, and type 2 diabetes mellitus. He was using amlodipine + valsartan 10/160 mg/day, vildagliptin 50 mg/day, nebivolol 5 mg/day peroral. In November 2020, cisplatin gemcitabine was started with the diagnosis of lung squamous cell carcinoma, weekly paclitaxel (80 mg/m^2) chemotherapy was started due to progression. He received two doses of CorovaVac during his weekly paclitaxel chemotherapy. The RBD IgG level measured on day 31 after the second vaccine dose was 4.8 AU/mL (negative). About five months after the second dose of the vaccine, he presented to the emergency department with the complaint of shortness of breath. SARS-COV-2 Delta variant was detected in his PCR test, and he died due to COVID-19 on day 19 of his hospitalization.

Discussion and conclusion

This study aimed to compare the efficacy and safety of the CoronaVac vaccine in breast and lung cancer patients receiving the active systemic therapy with the non-cancer population. After two doses of the CoronaVac vaccine, SARS-COV-2 Receptor binding domain (RBD) specific IgG positivity was 93.8 % in the control group and 81.6% in the cancer patients (p=0.005). No grade 3 or grade 4 adverse events were observed in either group. In the multivariate analysis of all the participants, being over 60 years of age (OR: 0.447, 95%CI: 0.218–0.917, p=0.010) and being a cancer patient receiving an active chemotherapy (OR: 0.303, 95%CI: 0.123–0.750, p=0.010) was associated with a low antibody response to the vaccine. During the median 124-day period until the third dose of vaccine (booster vaccine), three active COVID infections were seen in the cancer group, and 2 of these patients died due to COVID-19. There was no antibody response in the blood of 2 patients, who died after the second dose of CoronaVac. No active COVID-19 infection was detected in the control group during the median follow-up period of 129 days. These results showed that the CoronaVac vaccine is associated with a low antibody response in the cancer patients receiving the active systemic therapy, suggesting they are at higher risk than the non-cancer population in long-term follow-up.

Preliminary data of prospective randomized studies on the efficacy of the mRNA-1273 vaccine developed with different techniques in the cancer patients receiving the systemic therapy compared to the overall population has begun to be obtained (26). However, there is an insufficient data on the efficacy and safety of inactivated COVID-19 vaccines in cancer patients receiving systemic therapy. In the single-arm study on 47 cancer patients receiving systemic treatment, Karacin et al determined the seroconversion rate as only 59.5 % after vaccination (23). In the phase 4 study by Medeiros-Ribeiro et al, lower anti-SARS-CoV-2 IgG seroconversion was observed in immunocompromised rheumatologic patients than in healthy volunteers (70.4 % vs 95.5 %, p<0.0019). In our study, RBD-specific IgG seroconversion was 93.8 % in the control group in 28±3.1 days after two doses of CoronaVac vaccine, but this rate was 81.6 % in the cancer patients receiving systemic therapy (p=0.005).

In the participants' 2-dose post-vaccination follow-ups, two cancer patients aged 72 and 85 years with no RBD-specific IgG response died of COVID-19 pneumonia. COVID-19 treatment of a 51-year-old cancer patient with an antibody level of 876.3 AU/mL was completed at home. No case of COVID-19 infection was

detected in the control group. To the best of our knowledge, this study is the first two-arm study to compare two doses of vaccine in the cancer patients receiving systemic therapy with the non-cancer population and share long-term results.

There are some limitations to our study. Pre-vaccination blood RBD IgG levels or nucleocapsid proteins were not measured serologically. Therefore, this study does not definitively assess pre-vaccination COVID-19 disease. The pre-vaccination antibody or PCR measurements are not routinely recommended under national vaccination programs, so our study had a real-life experience simulation design. Another limitation is that neutralization antibodies were not measured. However, RBD IgG antibodies provide a high degree of neutralization and correlate with neutralizing antibody levels (27).

In conclusion, in the cohort of 201 breast and lung cancers, the RBD IgG antibody response rate was 81.6 % (93.8 % in 97 controls) after two doses of CoronaVac, and the antibody titer was significantly lower than in the control group. In post-vaccination follow-ups, 2 of the patients in the cancer group died due to COVID-19, and one survived COVID-19. Our findings showed that cancer patients over 60 years of age receiving the systemic therapy are still at high risk for COVID-19 despite the CoronaVac vaccine and suggest that additional protective measures should be taken for these patients.

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