IMMUNOGENICITY AND SAFETY OF THE CORONAVAC INACTIVATED VACCINE IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: A PHASE 4 TRIAL

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BACKGROUND

CoronaVac, an inactivated SARS-CoV-2 vaccine, has been largely used as the main emergency-based approved immunogen for COVID-19 in several countries. However, its immunogenicity in immunocompromised individuals has not been established. The objective is to evaluate the immunogenicity and safety of CoronaVac in patients with autoimmune rheumatic diseases (ARD).

METHODS

We initiated a prospective phase 4 controlled trial (NCT04754698, CoronavRheum) of 910 adults with ARD and 182 age- and sex-frequency matched healthy adults (control group, CG) who received two doses of CoronaVac (28-day interval). Both groups had negative serology and neutralizing antibodies for COVID-19 at baseline. Anti-SARS-CoV-2 S1/S2 proteins IgG (DiaSorin) and neutralizing antibodies (NAb) (GenScript) were assessed prior to each vaccine shot (D0 and D28) and 6 weeks after the 2nd dose (D69). Patients of ARD and CG groups were evaluated using COVID-19 symptoms and adverse events (AE) diaries, three face-to-face visits, and 24-h available phone, WhatsApp and e-mail contact. Symptomatic cases were tested by RT-PCR for SARS-CoV-2 and a subgroup of positive samples were evaluated for the presence of variants of concern. The primary outcomes were presence of anti-SARS-CoV-2 IgG and NAb 6 weeks (D69) after the 2nd dose. Secondary outcomes were geometric mean titers (GMT) and factor increase in GMT (FI-GMT) of anti-SARS-CoV-2 IgG, median (interquartile) percentage of neutralizing activity of NAb and vaccine safety.

RESULTS

Prespecified end-points were met, with lower anti-SARS-CoV-2 IgG seroconversion (70.4% vs. 95.5%, $p < 0.001$) and titers (12.1 [95%CI = 11.0–13.2] vs. 29.7 [95%CI = 26.3–33.5], $p < 0.001$), frequency of NAb (56.3% vs. 79.3%, $p < 0.001$) and median (interquartile range) neutralization activity (58.7 [43.1–77.2] vs. 64.5 [48.4–81.4], $p = 0.013$) in patients with ARD compared to CG at D69. Age ≥ 60 years old and use of prednisone were associated to lower immunogenicity both to IgG and NAb. Among the immunosuppressive drugs, methotrexate and mycophenolate mofetil had the most negative impact on immunogenicity, whereas rituximab, abatacept and TNFi were the most negative among those treated with biologics. Vaccine safety analysis revealed similar AE between the groups, with no moderate/severe event. A significant decline in the number of COVID-19 cases ($p < 0.0001$) was observed 10 days after the second dose, with a predominant gamma variant. Four ARD patients were hospitalized and none deceased due to COVID-19.

CONCLUSION

CoronaVac has an excellent safety profile and induces moderate IgG seroconversion and neutralizing antibodies in the majority of patients with ARD.

KEYWORDS

Autoimmune rheumatic diseases, COVID-19, Vaccine, Immunogenicity, Safety.