Humoral and Cellular Immunogenicity and Safety of 3-Dose Inactivated COVID-19 Vaccine in Young Children Less Than 5 Years With Kidney Diseases

To the Editor: There are no available data pertaining to humoral and cellular responses against COVID-19 among young children with kidney diseases after inactivated vaccine.[1] We therefore evaluated the immunogenicity and safety of 3-dose CoronaVac at an accelerated schedule (0.5 ml; days 0, 14, and 28) in a prospective study in Hong Kong (COVAC; NCT04800133) (Supplementary Methods).[2]

A total of 64 children were enrolled, and 5 young children (median age 3.3 years, interquartile range 3.1–3.6; 3 females; 3 Chinese) were analyzed (glomerular disease on immunosuppression, $n = 2$; advanced chronic kidney disease, $n = 2$; kidney failure, $n = 1$) (Supplementary Table S1).

We tracked antibody responses in our patients against wild-type SARS-CoV-2, including S-RBD IgG for binding antibody and surrogate virus neutralization test for neutralization longitudinally from prevaccine baseline to post-dose 3 (Figure 1a and b).[3] After 3 doses, all were seropositive for S-RBD IgG and had a high geometric mean surrogate virus neutralization test percentage level of 94.0%, with increases in titers after successive doses.

We also studied IFN-γ^+ antiviral $CD4^+$ helper and $CD8^+$ cytotoxic T-cell responses against SARS-CoV-2 S, N, and M proteins (Figure 2a-d). We detected a significant increase of SNM-specific IFN-γ^+ $CD4^+$ T-cell response in all 5 patients (Figure 2b). Other T-cell responses such as IL-2 also had an increasing trend (Supplementary Figure S1A–D). Importantly, all had S-specific or SNM-specific IFN-γ^+ $CD4^+$ and $CD8^+$ T-cell responses.

When compared with wild-type antibody response, we found a significantly lower surrogate virus neutralization test percentage level against Omicron BA.1 (post-dose 3, 94.0% vs. 17.9%, $P = 0.0012$) (Supplementary Figure S2A), indicating partial neutralization escape. Nonetheless, IFN-γ^+ T-cell responses were similar between Omicron BA.1 and wild type (Supplementary Figure S2B–D).[4]

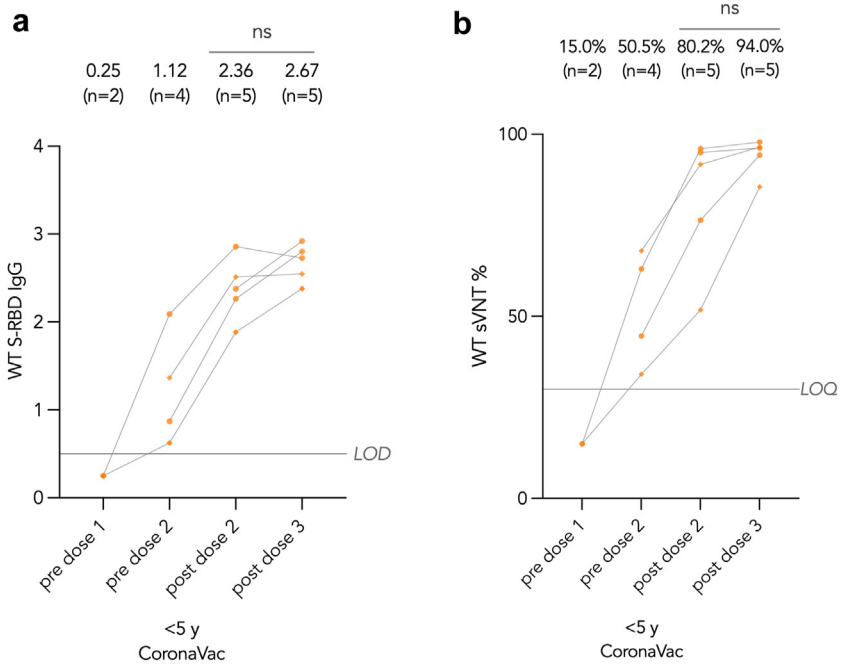

Figure 1. Antibody responses against wild-type SARS-CoV-2 including (a) S-RBD IgG for binding and (b) sVNT for neutralization. Matched post-dose 2 tests were compared with post-dose 3 by paired *t* test after natural logarithmic transformation, and *P* values are denoted by asterisks (ns, not significant). GM were stated above each column. LOD and LOQ were drawn as gray lines. Datapoints from patients who were on immunosuppression were depicted as rhombi. GM, geometric means; LOD, limit of detection; LOQ, limit of quantification; ns, not significant; sVNT, surrogate virus neutralization test.

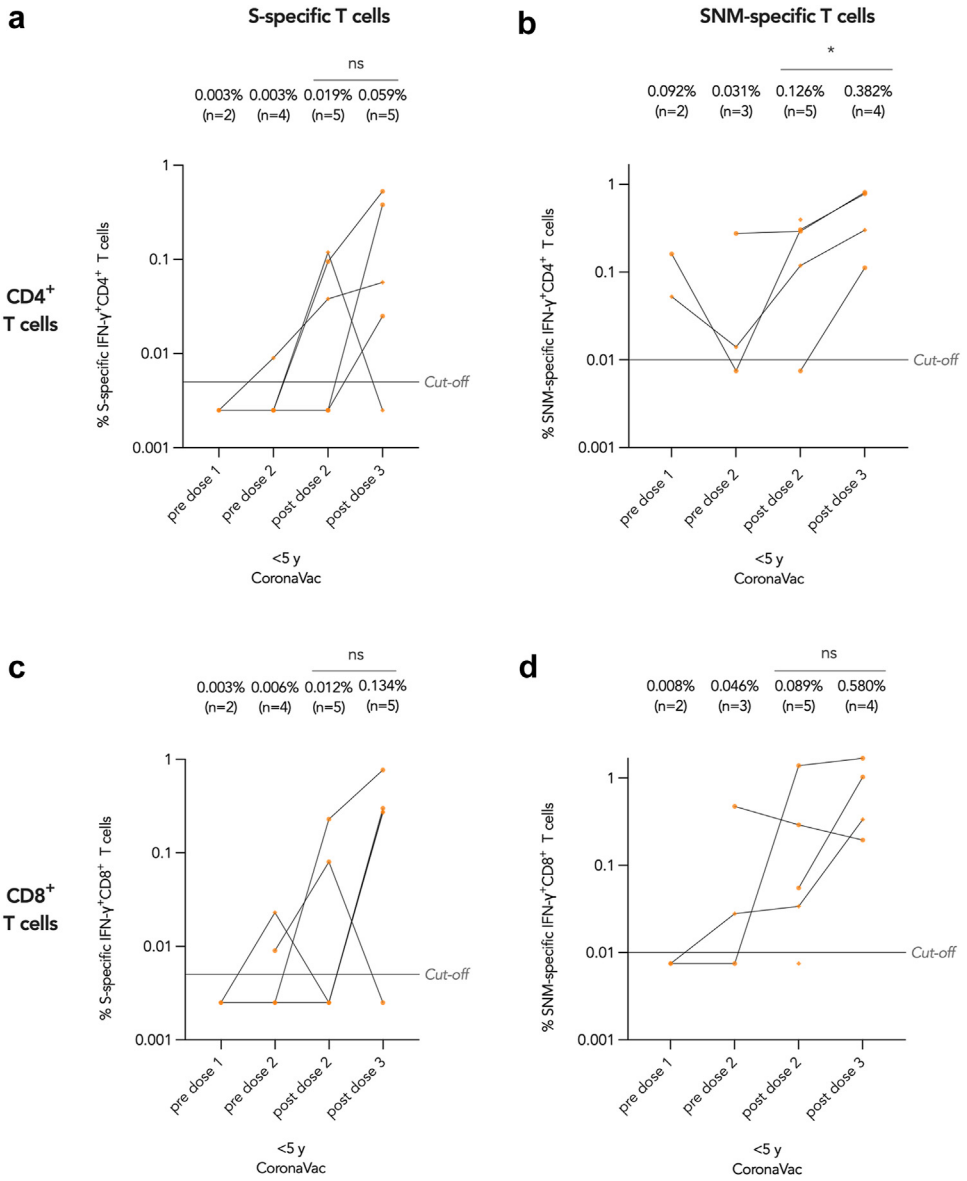

Figure 2. IFN- γ^+ T-cell responses against wild-type SARS-CoV-2 proteins. T-cell responses against S, N, and M proteins were tested for all participants. Matched post-dose 2 and post-dose 3 tests were compared by paired *t* test after natural logarithmic transformation, and *P* values are denoted by asterisks (*, $P < 0.05$). GM were stated above each column. Cutoffs were drawn as gray lines. Datapoints from patients who were on immunosuppression were depicted as rhombi. Refer to Supplementary Figure S5 for gating strategy. GM, geometric means; ns, not significant.

In addition, we noticed comparable antibody responses between these 5 patients and healthy subjects aged 3 to 5 years who were recruited in another subgroup of the same prospective study (Supplementary Figure S3A and B). We also found that CoronaVac was safe and tolerable in our patients, and no breakthrough infections were reported after a median of 118 (interquartile range 111–132) days after dose 3 (Supplementary text 1 and Supplementary Figure S4).

In conclusion, we revealed that accelerated, 3-dose CoronaVac vaccination was safe and elicited satisfactory antibody and T-cell responses in young children with kidney diseases. T-cell responses seemed preserved against Omicron BA.1, which prevents severe COVID-19.

DISCLOSURE

The authors declared no competing of interests.

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DATA SHARING

All requests to share the pseudonymized data underlying the conclusions of this paper from researchers will be facilitated by the authors, subject to ethics approval. Enquiries should be addressed to lauylung@hku.hk.

AUTHOR CONTRIBUTIONS

YLL conceptualized the study. YLL, MP, WT, DL, JSRD, and XM designed the study. YLL led the acquisition of funding. YLL, WT, and MP supervised the project. SMC, DL, XM, SMSC, IYST, and JHYL led the study administrative procedures. AL-TM, YLL, JSRD, EY-HC, SC, FT-WH, P-CT, W-ML, and MHLL provided study-related clinical assessments and follow-up. DL, SMC, STKS, JHYL, JSRD, and YLL collected clinical safety data. SMSC, LCHT, KKHK, and MP developed and performed S-RBD IgG and sVNT. XM, YC, HHWW, AMTL, WYL, and WT developed and performed the T cell assays. DL, DHLL, and JHYL curated, analyzed, and visualized the data. DL, XM, SMSC, JSRD, DHLL, JHYL, and SMC validated the data. DL and EY-HC drafted the manuscript and were supervised by AL-TM, JSRD, and YLL, with input from XM and SMSC. All authors reviewed and approved the final manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Supplementary Text.

Table S1. Demographics of young children <5 years receiving 3-dose inactivated COVID-19 vaccination.

Figure S1. IL-2^{+} T-cell responses against wild-type SARS-CoV-2 proteins.

Figure S2. Antibody and T-cell response against Omicron BA.1.

Figure S3. Antibody responses compared between patients and healthy children aged 3 to 5 years in our study.

Figure S4. Adverse reactions (ARs) and antipyretic use reported 7 days after each dose by vaccine type.

Figure S5. Gating strategy.

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