

ONLINE SUPPLEMENTARY MATERIAL

A RCT of a third dose CoronaVac or BNT162b2 vaccine in adults with two doses of CoronaVac

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Cohort study design and participants. 376 healthy adults aged between 19-77 years old who had received two doses of CoronaVac were recruited for our previous study in Hong Kong SAR, China at the community vaccination centers at the Chinese University of Hong Kong Medical Centre, Prince of Wales Hospital and Kowloon Bay Vaccination Station between March 10 and August 31, 2021 (1). 16 participants withdrew from the study. The percentage (%) inhibition of binding of SARS-CoV-2 spike receptor binding domain (RBD) to the ACE-2 receptor was tested by surrogate virus neutralization test (sVNT) in the plasma of 360 participants (1). Based on the previous study of convalescent antibody titers of RT-PCR confirmed convalescent symptomatic patients, we have estimated that the 20% convalescent antibody titer threshold for 50% protection from re-infection for PRNT₅₀ was 1:25.9 (95% CI 1:24.7-1:27.6) (2). Since there will be waning of antibody from the peak titres observed at 1-month post second dose of vaccine, we set the target titre to be achieved at 1 month post-second dose of vaccine to be twice the 50% protection titre, i.e 1:52. This corresponds to a sVNT inhibition of 60% (1, 2). 230 out of 360 in our cohort showed the sVNT results below 60% in their plasma specimens which were collected at one month after the second dose. Eighty participants of age between 34-73 years old were randomly selected and invited to join our third dose RCT between August and October, 2021. The participants were randomized to receive either BNT162b2 (n=40) or CoronaVac (n=40) as the third dose. Safety assessment objectives included recording of local or systemic reactogenicity events from each participant at 1 week of vaccination. Ten ml of heparinized blood were collected from each donor before vaccination and at one month after receiving the third dose of either BNT162b2 or CoronaVac.

Study approval. The study was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (Ref no: 2020.229) and all participants provided written consent. This clinical trial has been registered at ClinicalTrials.gov with identifier NCT04611243

Statistical analysis. Continuous variables were summarized as mean with SD while categorical variables were summarized as frequency. Geometric means were used for comparison of neutralization titers. Comparison between groups was conducted with the nonparametric Mann-Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables as appropriate. All analyses were performed in R (version 4.1.0; R

Foundation for Statistical Computing) or Prism 9 (Graphpad). P values < 0.05 were considered statistically significant.

Role of the funding source. The sponsor of the study played no role in study design, data collection, data analysis, data interpretation, writing of the report or in the decision to submit this manuscript for publication. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

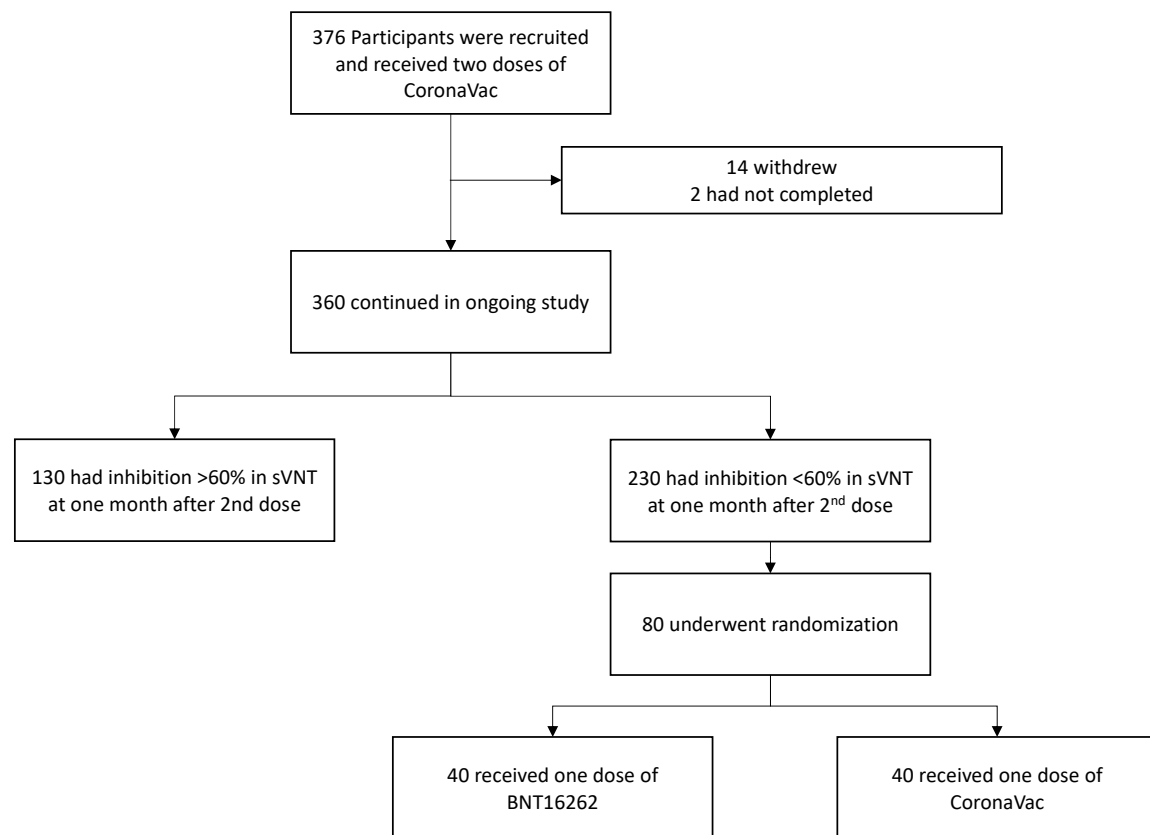
Acknowledgments

We acknowledge the technical support from Mr Huibin Lv and Mr Ho Lun Lai. We also thank Dr Fung Hong (Chinese University Medical Center), Dr Ken Tsang (Kowloon Bay community vaccination center) and Dr Beatrice Cheng (Prince of Wales Hospital) for allowing us to recruit subjects for this study. The recombinant RBD and NTD proteins were kindly provided as gifts by Prof Ian A. Wilson and Dr Meng Yuan from the Scripps Research Institute.

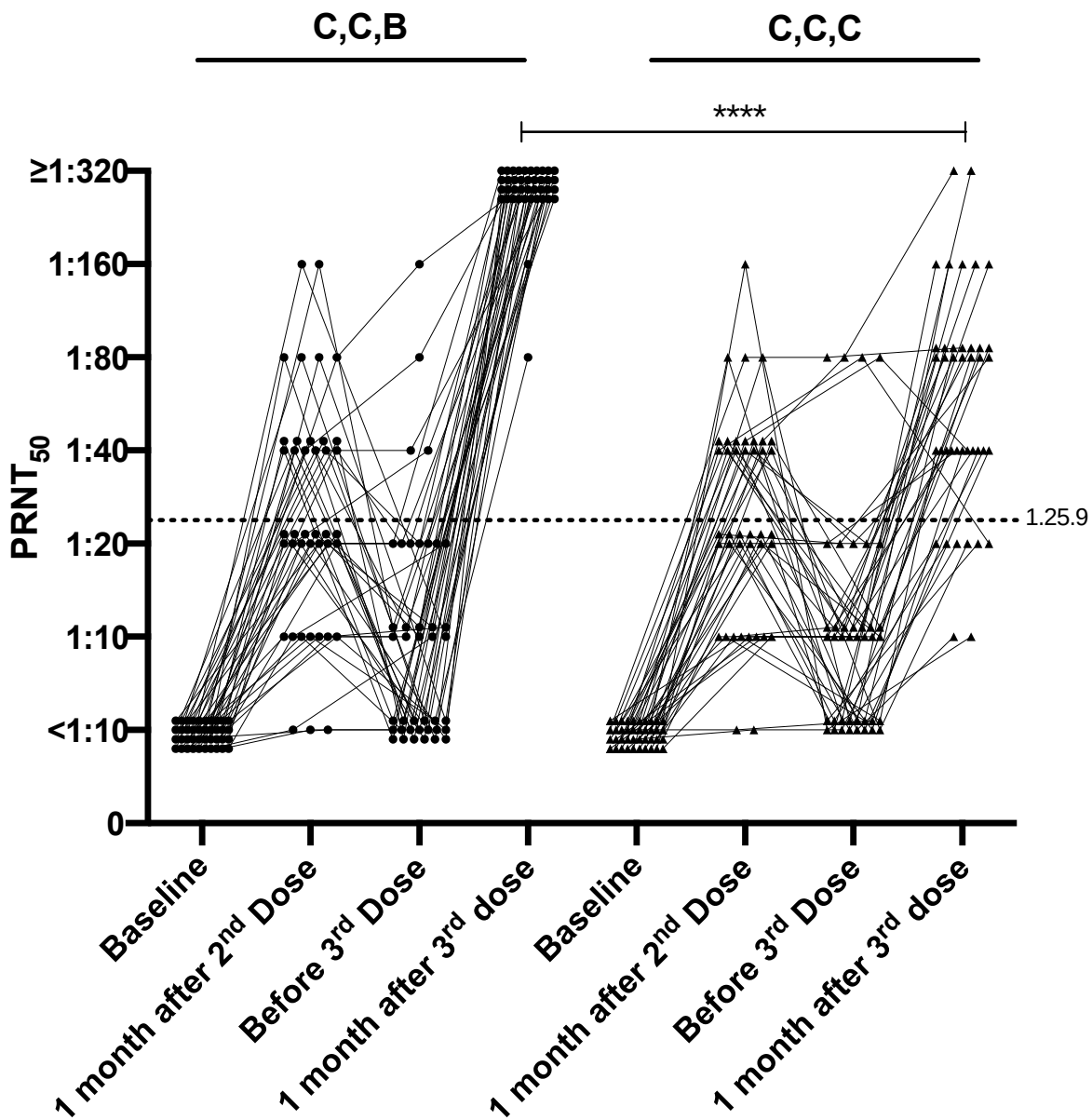
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Supplementary Figure 1. Flow chart of the randomized clinical trial study.



Supplementary Figure 2. Antibody responses of individuals before and after the third dose of either BNT162b2 or CoronaVac. The PRNT₅₀ after the third dose of either BNT162b2 (n=40) or CoronaVac (n=40) were detected from the plasma collected from vaccinated adult individuals who had received two doses of CoronaVac. The titers have been jittered to avoid overlap. Dotted line denotes the threshold for protection of 50% of individuals from infection. C,C,B and C,C,C indicate the vaccines (C: CoronaVac; B: BNT162b2) that were used for the first, second and third dose of vaccination. Comparison between groups were analyzed by the nonparametric Mann-Whitney U test. **** indicates p<0.0001



Supplementary Table 1. Demographic Characteristics of the Participants.

	C,C,B	C,C,C	
N	40	40	p-value
Days between 1 st and 3 rd dose	126.75	128.75	0.729*
Days between 2 nd and 3 rd dose	97.95	99.35	0.806*
Smoking			1.000
Yes	2	2	
No	38	38	
Alcohol Consumption			0.650
Never	25	22	
Sometimes	15	18	
Often	0	0	
Comorbidities			
Cardiovascular disease	0	3	0.241
Diabetes	2	2	1.000
Chronic respiratory diseases	2	2	1.000
Others	0	0	1.000
Resting			0.587 [#]
Regular	12	16	
Always insomnia / sleep late	6	4	
Sometimes insomnia / sleep late	22	20	
Regular Exercise			1.000
Yes	22	23	
No	18	17	
Flu vaccine			1.000
Yes	29	29	
No	11	11	
Hepatitis A/B vaccine			0.482
Yes	16	12	
No	24	28	

C,C,B and C,C,C indicate the vaccines (C: CoronaVac; B: BNT162b2) that were used for the first, second and third dose of vaccination. The comparison was analyzed by Fisher's exact test unless it is marked with * (Mann-Whitney U test) or [#] chi-square test.