Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19

We report here comparative data on SARS-CoV-2 vaccine immunogenicity in health-care workers in Hong Kong who received either the BNT162b2 vaccine (Comirnaty; Fosun–BioNTech) or the inactivated virus (vero cell) vaccine (Coronavac; Sinovac). We collected blood samples before vaccination, before the second dose, and 21–35 days after the second dose. We tested the samples for antibodies to SARS-CoV-2 using an ELISA to detect antibodies that bind to the receptor binding domain of the spike protein, testing ELISA-positive samples for neutralising antibodies with a surrogate virus neutralisation (sVNT) assay, and then a plaque reduction neutralisation test (PRNT) with live SARS-CoV-2 virus.[1,2]

We enrolled a cohort of 1442 health-care workers from public and private hospitals and medical clinics in Hong Kong and arranged for longitudinal collection of blood samples after obtaining informed consent. Here we present our preliminary laboratory testing results on 93 participants for whom we have complete data on antibody concentrations before vaccination, after the first dose, and after the second dose. These included 63 participants (55·6% male, median age 37 years, range 26–60 years) who were fully vaccinated with the BNT162b2 vaccine and 30 participants (23·3% male, median age 47 years, range 31–65 years) who received both doses of the inactivated vaccine.

In health-care workers who received the BNT162b2 vaccine, antibody concentrations measured by ELISA and sVNT rose substantially after the first dose and then rose again after the second dose of vaccination (appendix). In a subset of 12 participants for whom we also had PRNT results, after the second dose the geometric mean $PRNT_{50}$ titre was 269 and the geometric mean $PRNT_{90}$ titre was 113. In contrast, the health-care workers who received the inactivated vaccine had low antibody concentrations by ELISA and sVNT after the first dose, rising to moderate concentrations after the second dose. In a subset of 12 participants, after the second dose, the geometric mean $PRNT_{50}$ titre was 27 and the geometric mean $PRNT_{90}$ titre was 8·4.

Neutralising antibody titres have been proposed as a correlate of protection for SARS-CoV-2 vaccines.[3–5] The difference in concentrations of neutralising antibodies identified in our study could translate into substantial differences in vaccine effectiveness. Our study did not include data on other potential correlates of protection such as T cells or antibody-dependent cellular cytotoxicity. Future studies could investigate alternative strategies to increase antibody concentrations and clinical protection in recipients of inactivated vaccines, including administration of booster doses.

This work was supported by the Health and Medical Research Fund, Food and Health Bureau, Government of Hong Kong (grant number COVID190119). BJC is supported by the AIR@innoHK programme of the Innovation and Technology Commission of the Government of Hong Kong. BJC reports honoraria from Sanofi Pasteur, GlaxoSmithKline, Moderna, and Roche. All other authors report no other potential competing interests.

Wey Wen Lim, Loretta Mak, Gabriel M Leung, Benjamin J Cowling, Malik Peiris
bcowling@hku.hk

WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong Special Administrative Region, China (WWL, LM, GML, BJC, MP); Laboratory of Data Discovery for Health, Hong Kong Science and Technology Park, New Territories, Hong Kong Special Administrative Region, China (GML, BJC); HKU-Pasteur Research Pole, The University of Hong Kong, Pokfulam, Hong Kong Special Administrative Region, China (MP); Centre for Immunology and Infection, Hong Kong Science and Technology Park, New Territories, Hong Kong Special Administrative Region, China (MP).

1 Perera RA, Mok CK, Tsang OT, et al. Serological assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), March 2020. *Euro Surveill* 2020; **25:** 2000421.

2 Perera RAPM, Ko R, Tsang OTY, et al. Evaluation of a SARS-CoV-2 surrogate virus neutralization test for detection of antibody in human, canine, cat, and hamster sera. *J Clin Microbiol* 2021; **59:** e02504–20.

3 Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021; published online May 17. https://doi.org/10.1038/s41591-021-01377-8.

4 Koch T, Mellinghoff SC, Shamsrizi P, Addo MM, Dahlke C. Correlates of vaccine-induced protection against SARS-CoV-2. *Vaccines (Basel)* 2021; **9:** 238.

5 Earle KA, Ambrosino DM, Fiore-Gartland A, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. *Vaccine* 2021; **39:** 4423–28

Lancet Microbe 2021

Published **Online** July 15, 2021 https://doi.org/10.1016/S2666-5247(21)00177-4

This online publication has been corrected. The corrected version first appeared at thelancet.com/microbe on August 4, 2021

See **Online** for appendix