National Centre for Infectious Diseases

FOR IMMEDIATE RELEASE

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Using the Moderna vaccine (mRNA-1273) as a Booster Shot Induces a Stronger Antibody Response against the Omicron Variant in Older Adults: NCID Study

1. Interim findings from a local randomised clinical trial (RCT) 'Efficacy of Different COVID-19 Vaccine Combinations in Inducing Long-term Humoral Immunity', also known as ***PRIBIVAC***, have shown that antibody levels against COVID-19 were significantly higher in older adults (≥60 years old) who received a 'heterologous' booster shot with Moderna as compared with a 'homologous' booster shot with Pfizer-BioNTech/ Comirnaty.

2. The clinical trial led by the National Centre for Infectious Diseases (NCID) and conducted between 12 October and 3 December 2021 involved 100 participants[1] who had received the Pfizer-BioNTech/ Comirnaty as their primary series of COVID-19 vaccination. Of the first 100 participants, half are aged under 60 years old, while the other half are above 60.

3. These participants were randomly assigned to receive either Moderna (heterologous vaccine) or Pfizer-BioNTech/ Comirnaty (homologous vaccine) as a booster shot. Blood samples were collected pre-booster (day -28 to day 0), on day 7, and on day 28 post-booster for immunogenicity assessment.

4. Antibody levels prior to the booster shot were variable, tending to be lower with increasing age and among men. Most adults had low neutralising antibody levels against the Omicron variant regardless of age. However, vaccine antibody responses after the booster shot were uniformly excellent. On average, a 50-fold increase in spike antibody levels within one week after the booster shot was observed.

5. Researchers also found that antibody responses were significantly higher among older adults (60 years old and above) who received Moderna as a booster shot as compared with Pfizer-BioNTech/ Comirnaty. This includes antibody levels against the 'wild-type' SARS-CoV-2, and against all Variants of Concern (VOCs) – from Alpha to Omicron. Additionally,

    a. At Day 7 after booster shot, average antibody level was approximately twice as high with Moderna than Pfizer-BioNTech/ Comirnaty and 1.5 times higher at Day 28;
    b. Neutralising antibody level against Omicron with Pfizer-BioNTech/ Comirnaty was 72.8% at Day 28 versus 84.3% with Moderna.

6. In younger adults, antibody levels were similar whether a participant had received Moderna or Pfizer-BioNTech/Comirnaty as a booster shot.

[1] Two participants withdrew from the study eventually, resulting in an analysis sample size of 98.

7. These observations complement studies from other international trials and provide reassuring local data that a third dose of mRNA vaccine is safe and effective at boosting the immune response.

8. Dr Barnaby Young, Head, Singapore Infectious Disease Clinical Research Network (SCRN), NCID, who is leading the trial, said, "Based on interim results from the *PRIBIVAC* study, we know that although the Omicron variant is able to escape immunity among fully vaccinated individuals, taking Pfizer-BioNTech/ Comirnaty or Moderna as a booster shot helps increase the serum neutralising activity against Omicron by more than 50 per cent by Day 7 post-booster. The magnitude of the antibody boost is likely to offer significant protection against infection with this variant. Individuals at higher risk of severe COVID-19 such as older adults (60 years old and above) are more likely to have low antibody levels six months after primary vaccination series, so it is important that this group receives a booster shot."

9. Added Dr Young, "Taking Moderna as a booster shot may offer better or longer protection for older adults as well, as our research has observed a higher anti-spike antibody titer and a stronger neutralising response of the vaccine against the Omicron variant. The emergence of variants capable of evading protective immunity remains a concern and highlights the need for a long-term COVID-19 immunisation strategy. We hope *PRIBIVAC* will help to build local data on understanding immunity towards COVID-19 through booster shots."

10. The study also revealed that vaccine reactions were common, but were mild and short-lived. Common vaccine reactions were pain at the injection site within 72 hours of a booster shot, fatigue, followed by muscle pain. In the older age group (60 years old and above), fever and weakness occurred more frequently in those that received Moderna as a booster dose. No participant had a serious side effect.

11. Interim findings from *PRIBIVAC* were published today in a preprint in SSRN[2]. The clinical trial is supported by the Agency for Science, Technology and Research (A*STAR), Duke-NUS Medical School, and Singapore Clinical Research Institute (SCRI), and funded by grants from the National Research Foundation, Singapore and Ministry of Health, and administered by the National Medical Research Council (NMRC).

Next steps for *PRIBIVAC*

12. This study will continue to follow participants to monitor waning of antibody levels after the booster shot, with additional blood samples collected after six months and one year.

13. The next phase of *PRIBIVAC* is currently taking place. Commencing on 3 January 2022, up to 200 participants who earlier received either the Pfizer-BioNTech/ Comirnaty or Moderna as their primary series will be enrolled and randomly allocated to receive either Pfizer-BioNTech/ Comirnaty, Moderna or Covaxin vaccine as a booster shot. This means that in total six vaccination arms are now currently being studied as part of *PRIBIVAC* (i.e. PPP, PPM, PPC, MMP, MMM, and MMC).

14. The clinical trial is planned to extend to other vaccines in the future (including Nuvaxovid) to study how the antibody and cellular levels change with time. This will allow for novel data to be generated, to assess if using a heterologous booster vaccine provides a broader immune response against the Omicron variant and future COVID-19 variants. Up to 600 participants may be enrolled in *PRIBIVAC*, with a good range of age and ethnicities, to reflect Singapore's population.

[2] Preprint in SSRN - https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4056669

Annex A: Additional information on *PRIBIVAC*

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About the National Centre for Infectious Diseases

The National Centre for Infectious Diseases (NCID) is a purpose-built facility designed to strengthen Singapore's capabilities in infectious disease management and prevention. NCID houses clinical services, public health, research, training and education and community engagement functions under one overarching structure. In addition to the clinical treatment of infectious diseases and outbreak management, the expanded roles and functional units of NCID include the National Public Health and Epidemiology Unit, the National Public Health Laboratory, the Infectious Disease Research and Training Office, the Antimicrobial Resistance Coordinating Office, and the National Public Health programmes for HIV and Tuberculosis. Benchmarked to international standards and best practices, NCID will enhance Singapore's ability to effectively manage infectious diseases.

Visit www.ncid.sg for more information.

ANNEX A

Additional information on *PRIBIVAC*

This clinical trial helps build local data on understanding immunity towards COVID-19 through booster shots.

PRIBIVAC aims to:

1. obtain local data on vaccine response after homologous or heterologous mRNA booster shots, and examine how the immune response from these booster shots changes over the months after vaccination;
2. study non-mRNA vaccines (such as Covaxin) and determine if the antibody levels after the booster shot with these vaccines are similar to mRNA vaccines;
3. compare the immune response between homologous and heterologous booster shots and test the hypothesis that giving a heterologous booster might improve vaccine responses against variants as compared to the wildtype vaccine strain of SARS-CoV-2.

To participate in PRIBIVAC, healthy participants must be above 21 years of age and have received the second dose of the COVID-19 vaccine at least six months before enrolling in the trial. Additional criteria include not previously infected with COVID-19 and not pregnant or breastfeeding.

For those keen to participate in *PRIBIVAC*, please email scrn@ncid.sg or call +65 8618 7400.