Memo

Use of Novavax (Nuvaxovid) COVID-19 vaccine as a heterologous booster: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	6 May 2022
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From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) advice about the use of Novavax COVID-19 vaccine (Nuvaxovid) as a heterologous booster.

Background and context

2. On 4 February 2022, Medsafe approved, with conditions, the Novavax COVID-19 vaccine (Nuvaxovid) for use as a 2-dose primary course for those 18 years of age or older.
3. Medsafe are currently reviewing an application from Novavax for the use of Nuvaxovid as a booster dose in New Zealand.
4. The Ministry of Health has asked CV TAG for advice on the use of Nuvaxovid as a heterologous booster (i.e., following a primary course of a different COVID-19 vaccine or vaccines) given that most New Zealanders have now received a primary course of the Pfizer COVID-19 vaccine.
5. CV TAG has previously recommended that a single additional dose of a Medsafe-approved vaccine can be used in a heterologous schedule to complete a *primary* course of vaccination for people who have arrived in New Zealand. This so that those vaccinated overseas with COVID-19 vaccines that do not have World Health Organisation Emergency Use Listing (as well as those who have not received a complete primary course of COVID-19 vaccine) can meet primary vaccination requirements in New Zealand. The full CV TAG recommendations are given in the CV TAG memo 'New Zealand definition of fully vaccinated for use inside the New Zealand border' dated 5 November 2021. CV TAG have now been asked to confirm that Nuvaxovid can be used in the same way as other Medsafe-approved vaccines to meet these requirements.
6. International peak bodies have recommended Nuvaxovid as a booster dose:

a. The Australian Technical Advisory Group on Immunisation (ATAGI) stated on 24 January 2022 that "Nuvaxovid (Novavax) can be used as a booster in an individual aged 18 years and above if no other COVID-19 vaccine is considered suitable for that individual." Note this is prior to Nuvaxovid being approved as a booster in Australia. [1]

b. The National Advisory Committee on Immunization (NACI, Canada) stated on 17 February 2022 that "Novavax (Nuvaxovid) may be used in a heterologous (mixed) primary series or as a booster dose in a heterologous prime-boost series for individuals for whom mRNA COVID-19 vaccine is contraindicated, inaccessible, or has been refused". [2]

c. The Joint Committee on Vaccination and Immunisation (JCVI, UK) and Advisory Committee on Immunization Practices (ACIP, USA) have not issued advice on the use of Nuvaxovid as a booster.

Data about Nuvaxovid as a Homologous booster dose

7. Due to evidence of waning vaccine efficacy, the suitability of Nuvaxovid as a homologous booster dose (after 2 primary doses of Nuvaxovid) was assessed in a 2021 study. Administration of a booster dose of Nuvaxovid approximately 6 months following the primary vaccination series resulted in an incremental increase in reactogenicity. [3]

8. Immune responses following the booster were notably higher than those associated with high levels of efficacy in phase 3 studies of the vaccine. [3] A receptor binding inhibition assay analysing activity against SARS-CoV-2 found 20.1-fold increases in titers against Omicron and 24.4-fold against Delta 189 days post booster. [3]

Data about Nuvaxovid as a heterologous booster dose

9. As Nuvaxovid has only recently become available for use around the world, less data is available for this vaccine than for many other COVID-19 vaccines. Most of the available data comes from the UK COV-BOOST study, a multicentre, randomised, controlled, phase 2 trial evaluating third dose booster vaccination against COVID-19. [4] Seven vaccines, including Nuvaxovid, were studied as boosters in the trial. Participants were ages 30 years and over and received a booster dose at least 84 days after a primary course of Pfizer or at least 70 days post a primary course of AstraZeneca, with no history of laboratory-confirmed SARS-CoV-2 infection.

Reactogenicity and Safety

10. This study indicated that in general, heterologous boosters of Nuvaxovid, Janssen, Moderna, Valneva, and CureVac are well-tolerated following a primary course of Pfizer or AstraZeneca. [4]

11. The most common adverse events were in those who had a different booster vaccine than what was used for the primary course. Fatigue and headaches were the most common systemic reaction amongst individuals with the most common local reaction being injection site pain. Participants primed with Pfizer reported more frequent local and systemic reactions after receiving a booster of AstraZeneca, Janssen, Moderna, or CureVac, when compared with other vaccines, including Nuvaxovid.

12. Participants aged 30-69 years experienced more adverse events than those aged 70 years or older. [4]. Individuals who received Nuvaxovid after Pfizer experienced mild side effects. [4]

13. For participants primed and boosted with Pfizer, adverse events were experienced by 29.4% (32/109) of those with a full dose booster, and 27.3% (30/110) of those with a half dose,

compared to those who received Nuvaxovid as a booster, with adverse events experienced by 38.6% (44/114) of those with a full dose booster, and 36.6% (41/112) with a half dose booster. [4]

14. Serious adverse events were uncommon and were similar in all control groups. [4] In total, there were 24 serious adverse events, five of which were in the control groups and the rest were balanced among different booster groups. Three of these were from the Pfizer primed group boosted with Nuvaxovid (two from the half dose and one from the full dose) and none were from the Pfizer primed and Pfizer boosted group. There are some limitations to this study. The study cohorts may not have been large enough to detect rare serious adverse events (e.g., myocarditis). In addition, the interval from second to third dose was not consistent among participants due to the ongoing pandemic changing timelines for vaccination.

15. For myocarditis after Nuvaxovid vaccination, the only data available are from the clinical trial of the primary course. [5] A total of three cases of myocarditis were reported in the two phase III trials, of which two occurred in the vaccine groups and one in the placebo groups. [5] Of the two cases in the vaccine groups, one was a young healthy participant with onset three days after the second dose, and the other was a participant aged over 65 years.

Immunogenicity

16. Data from the UK COV-BOOST trial show that the Nuvaxovid booster elicited a modest increase in neutralising antibody titres after a Pfizer primary course [4] (Figure 1, Airfinity). In comparison, booster doses of mRNA vaccines (Pfizer or Moderna) produced the highest levels of neutralising antibody after a Pfizer primary series.

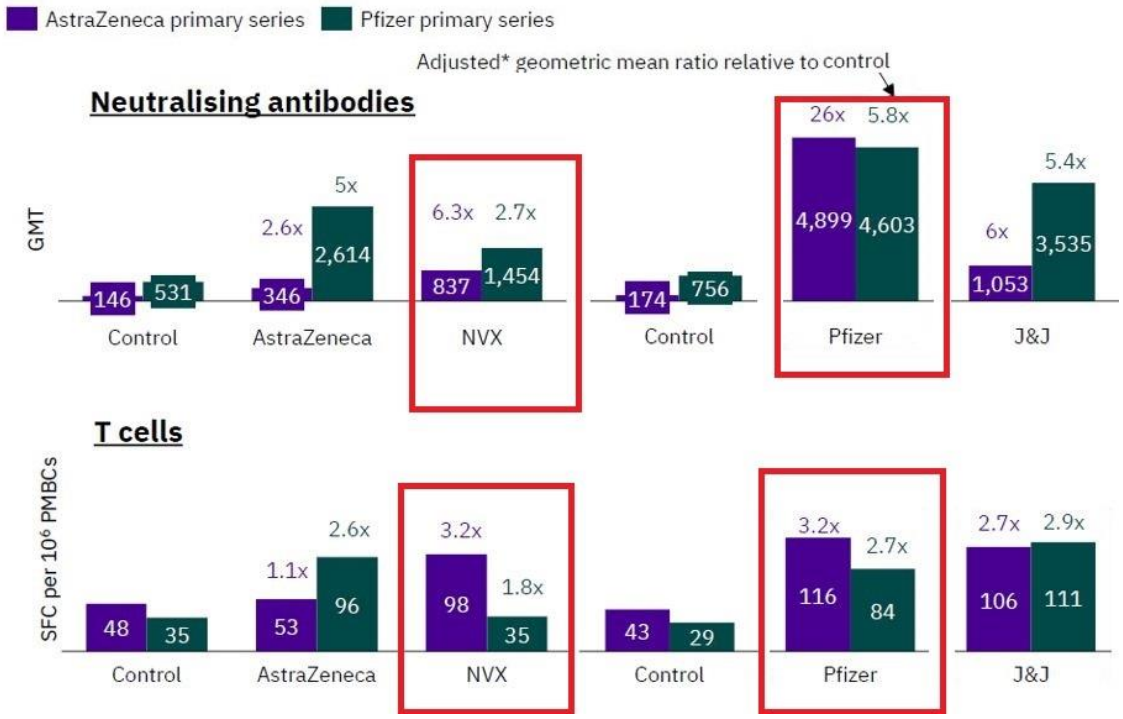

Figure 1. Immunogenicity results from UK COV-BOOST study (Source: Airfinity

*Adjusted for age group, site, baseline anti-spike IgG, interval between first and second dose, and interval between second and third dose

17. Immunogenicity results showed that the most consistent increase to neutralising antibodies and T cell responses (relative to control, adjusted) were induced by Pfizer, Moderna, and Janssen (Figure 1). For individuals primed with Pfizer, Nuvaxovid showed a 2.7x increase in

neutralising antibodies and a 1.8x increase in T-cell numbers. Individuals who were boosted with Pfizer which showed a 2.7x increase in T-cell numbers and 5.8x increase in neutralising antibodies.

Efficacy/Effectiveness

18. There are no data available about the efficacy of Nuvaxovid as a booster dose.

Recommendations

19. CV TAG met on 1 and 29 March 2022 to discuss the use of Nuvaxovid as a heterologous booster.

20. **CV TAG noted that:**

    a. Nuvaxovid is not yet approved for use as a booster by Medsafe.

    b. Data remain limited about the use of Nuvaxovid as a booster.

    c. Nuvaxovid boosters appear to be more reactogenic than Pfizer boosters.

    d. As limited data is available on mixed schedules with Nuvaxovid, **informed consent** should be a critical component of booster vaccinations and include a discussion of the benefits and risks of the mixed schedules with Nuvaxovid.

    e. Some of those receiving Nuvaxovid as a booster dose will be doing so after an adverse reaction to other COVID-19 vaccines. Because of this, caution should be exercised when recommending the interval between primary vaccination and the Nuvaxovid booster until more data abouts its safety profile in this group become available.

21. **CV TAG recommended that:**

    a. Pfizer remains the preferred booster vaccine for use in Aotearoa New Zealand.

    b. Nuvaxovid can be used on prescription as a booster dose if other available COVID-19 vaccines are not considered suitable for that individual. Nuvaxovid can be used a homologous or heterologous booster dose in those aged 18 years and over, and can be given from 6 months after the primary vaccine course. A shorter interval (from a minimum of 3 months after the primary course) could be considered in circumstances where the risk from SARS-CoV-2 infection is considered to be high and to outweigh any risk of a shorter interval, or where a booster is required to meet vaccination requirements (e.g. for work).

    c. Nuvaxovid can be used (in those aged 18 years and over) to complete a primary course of vaccination to meet vaccine requirements in New Zealand for those vaccinated overseas with any vaccine authorised by at least one government or authority, as described in the CV TAG memo 'New Zealand definition of fully vaccinated for use inside the New Zealand border' dated 5 November 2021.

    CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

Dr Ian Town

Chief Science Advisor and Chair of the COVID-19 Vaccine Technical Advisory Group

References

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