Appendix 1

SCIENCE & TECHNICAL ADVISORY | RŌPŪ TOHUTOHU I TE PŪTAIAO ME TE HANGARAU

MINISTRY OF HEALTH | MANATŪ HAUORA

Science Overview of Pfizer COVID-19 Vaccine

Contents

1. Prior COVID-19 infection

At least eight small studies have shown that those with previous COVID-19 disease produce a strong antibody response after a single dose of vaccine.[1-6] This response is similar in magnitude to that seen after two doses in those without prior COVID-19 disease. One of these studies also found that the SARS-CoV-2 infection also led to increased numbers of double negative B memory cells, which might be a "dysfunctional B cell subset".[1] One study has also shown that a single dose of Pfizer vaccination after infection with "original strain" virus substantially enhances neutralising antibody responses against variants including the Beta variant [7].Overall it has been suggested that vaccination following infection results in a broader and greater magnitude neutralising antibody response than vaccination in SARS-CoV-2 naïve individuals.[8]

Prior infection may also increase the durability of immunity. A Spanish study comparing antibody titres in previously infected and infection naïve healthcare workers found that at two months post-vaccination, the previously infected group had higher antibody titres.[9]

2. Immunogenicity

2.1. General

This vaccine is immunogenic. In 18-55 year olds, neutralising antibody levels were 3.8 times that in convalescent plasma 1 week after the second dose and in 65-85 year olds 1.6 times, with all vaccine recipients in both age groups producing detectable neutralising antibody titres.[10] Data from a phase 3 trial in adolescents (12-15 years of age) showed a strong neutralising antibody response to vaccination.[11]

In a (non-peer reviewed) observational study, uniformly robust IgG responses across all vaccinees were only seen after the second dose was administered.[12]

When comparing Pfizer vaccination with natural infection, a (non-peer reviewed) study found that vaccination generated lower levels of original antigenic sin-like antibodies and higher levels of SARS-CoV2 specific antibodies.[13] The implications of the cellular response to Pfizer are under-researched. However, a (non-peer reviewed) study monitoring cellular responses to vaccination in the 6-months after the second dose found CD4+ and CD8+ lymphocytes display features of polyfunctionality and longevity.[14]

2.2. Single-dose schedule

The neutralising antibody titres generated by one dose are significantly less than those generated after two doses. Furthermore, in the interdose period during an extended interval, neutralising antibody responses have been seen to wane following a peak at around 4 weeks, however the T cell response has been seen to persist. As with post two doses, there is variability seen in the magnitude of the antibody response after the first dose, with it generally higher in healthy younger adults, however there is limited data on whether the kinetics of the response are similar over the extended intervals.[15-20]

2.3. Extended interval two-dose schedule

Studies have found that extended intervals between the first and second dose produce higher peak spike-specific antibody responses (3.5-fold higher among 172 80+ participants with a 12-week interval,[21] and ~2-fold among 280 infection-naïve healthcare workers with a 6-14 week interval[16]). However, longer intervals were associated with lower peak T-cell responses when compared to the 3-week interval (3.6 fold in the 80+ group,[21] and 1.59-fold among healthcare workers[16]). Yet among the healthcare workers, the longer interval saw a greater proportion of the T cell response comprised by CD4+ cells and was suggestive of a more developed memory cell phenotype. There were no significant differences between the intervals for 223 previously infected healthcare workers in this study.[16] A Canadian (non-peer reviewed) study has also that found while delaying the second-dose reduced spike-specific CD4+ T-cell responses (>2-fold reduction in median T-cell frequency), anti-RBD binding titres were significantly elevated (3.3-fold increase).[22]

A UK (non-peer reviewed) study, in ages 50+, found that anti-S IgG titres were ~10x fold higher in those with a 65-84 day interval vs the regular 19-29 day interval.[23] Another UK study compared immunogenicity in adults after they received standard or extended-interval schedules of the Pfizer vaccine. They found that the extended interval was associated with higher neutralising antibody levels and an enrichment of CD4+ T cells expressing IL2.[24]

Some evidence suggests that the longer schedule may have a limited effect on the duration of immune response. A (non-peer reviewed) study of antibody responses following the second dose of Pfizer found that while shorter intervals were associated with a lower antibody response at day 21, however by day 42 they were similar to longer intervals. When analyses were limited to the <70 age group, there was no difference between short and extended intervals.[25]

A Canadian (non-peer reviewed) study found that a 16-week interval generated a similar neutralising antibody response to those who had been previously infected and received one dose.[26]

3. References

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