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Correspondence and Replies

How important is the second dose of the COVID-19 mRNA vaccine?



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Conflicts of interest: The author declares no relevant conflicts of interest.

Received for publication February 6, 2021; accepted for publication February 8, 2021.

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To the Editor:

The current data and lack thereof for allergy guidance on coronavirus disease 2019 (COVID-19) mRNA vaccines was outlined beautifully by Banerji et al¹ and Greenhawt et al.² As allergists create algorithms and testing protocols to evaluate patients who have had possible allergic reactions to the first dose of the Pfizer/BioNTech or Moderna vaccine, it also falls to allergists to counsel patients on the undefined benefit of the second dose.

Booster doses are intended to promote B-cell affinity maturation, increase neutralizing antibodies, and expand the memory T-cell pool. In practice, both COVID-19 mRNA vaccines confer excellent short-term protection starting 2 weeks after the first dose, before second-dose administration. Between days 15 and 21 after the first dose, symptomatic infections were reduced by almost 90% among Pfizer trial participants.³ Among Moderna trial participants who received a single dose only, vaccine efficacy was 92% starting at day 14, with a median follow-up of 28 days.⁴ Efficacy might suffer against variants such as B.1.351, and whether this difference would be affected by delaying a second dose is unknown.

In the short-term, the infection-related risk of delaying a second dose of mRNA vaccine by several weeks may be low. For those who experience a possible first-dose reaction, such a delay may allow patients time to gather information to guide a second-dose decision. Studies are ongoing on degree and duration of protection with a single dose, safety and efficacy of mixing vaccines (eg, adenovirus vaccine after mRNA vaccine), and impact of vaccine intervals on protection against or development of new variants. As allergists pursue various evaluation algorithms, we will find out more about the predictive value of skin testing, likelihood of second reactions, and efficacy of vaccines given by graded challenge.

Adenovirus vector vaccines may change allergists' algorithms. Johnson & Johnson has obtained emergency use authorization for its vaccine as a single dose, and AstraZeneca's vaccine data are encouraging for single-dose efficacy for at least 3 months. Combined data from AstraZeneca trials showed vaccine efficacy of 76% after a single dose, with stable antibody titers to day 90, compared with 67% overall efficacy after 2 doses, with noted demographic differences between subgroups. Among those who received 2 doses, prolonging the interval between doses to 3 months was associated with greater vaccine efficacy, at 82% and 55%, with dose intervals of 12+ weeks and less than 6 weeks, respectively.⁵

Motivated patients seeking clearance for a second mRNA vaccine dose tell us they want this "life-saving" protection. Yet we do not know whether the second dose confers substantial additional protection against hospitalization and death.

For the general population, both mRNA vaccine doses should be given as studied, supply permitting. For patients whose first-dose reactions have raised concerns about second-dose safety, the limited data on short-term single-dose efficacy should be weighed along with exposure risk and reaction severity.

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<https://doi.org/10.1016/j.jaip.2021.02.061>

Reply to "How important is the second dose of the COVID-19 mRNA vaccine?"



To the Editor:

We thank Liu¹ for a thoughtful commentary on recent guidance for coronavirus disease 2019 (COVID-19) vaccination.^{2,3} Liu¹ raises several important points that highlight uncertainties surrounding the COVID-19 vaccination effort, suggesting that for some patients who experience a severe allergic reaction to a first mRNA vaccine dose, a second vaccine dose may be deferred or delayed in light of limited evidence demonstrating good short-term efficacy of a single dose.^{1,4-6} Our understanding continues to rapidly evolve on this topic. For example, a recent study from the Sheba Medical Centre reported an 85% (95% CI, 71%-92%) reduction in symptomatic COVID-19 cases 15 to 28 days after the first dose of the Pfizer-BioNTech vaccine.⁵ This reduction in symptomatic COVID-19 infection is improved from an original estimate for first-dose vaccine efficacy of 52.4% reported by Polack et al,⁷ and may differ as a result of timing of the measurement. When considering the ratio of confirmed cases of COVID-19 illness in active versus placebo groups from Polack et al, Pfizer-BioNTech vaccine efficacy has been estimated at 92.6% beginning 14 days after dose 1 to before dose 2.⁶ Indeed, this rate is similar to the first-dose efficacy rate of 92.1% reported for the Moderna vaccine.^{6,8} Still, uncertainty remains regarding single-dose mRNA vaccine protection, as a recent population-based Israeli study including 596,618 vaccinated persons estimated single-dose effectiveness against documented infection at 14 to 20 days at 46% (95% CI, 40%-51%) for the Pfizer-BioNTech vaccine, with