Data Emerge From the UK’s COVID-19 Vaccine Extended Dosing Interval

Late last year, UK health authorities announced that the second dose of authorized COVID-19 vaccines would be administered up to 12 weeks instead of 3 to 4 weeks after the first dose. The change was intended to free up initial doses for more people, but it also created an opportunity to investigate a vaccine schedule that hadn’t been tested in clinical trials.

One resulting study, which has not yet been peer reviewed, found greater vaccine efficacy when the first and second BNT162b2 (Pfizer-BioNTech) vaccine doses were given more than 6 weeks apart. Another study, recently published in Cell, analyzed immune responses 4 weeks after the second BNT162b2 shot was administered to almost 600 UK health care workers, most of whom received the long-dosing regimen.

In the latter study, neutralizing antibody levels were higher after a 6- to 14-week dosing interval than after a 2- to 5-week interval, although the wait made less of a difference for workers with prior SARS-CoV-2 infections.

Compared with the short-interval group, SARS-CoV-2 spike protein-specific B-cell responses were about 7 times higher among participants in the long-interval group who hadn’t been previously infected. T-cell responses were robust in both groups, although infection-naive participants in the extended dosing group had fewer of a certain T-cell subset.

“When community levels of circulating SARS-CoV-2 virus are low, the extended dosing interval appears to be suitable for immunogenicity, but this needs to be weighed against the more immediate benefits of two doses over one,” the authors wrote.

They cautioned that participants’ responses were highly variable, so the findings are more relevant on a population level than an individual level. Ongoing studies will measure how long the workers’ immune responses persist after the extended regimen.

COVID-19 Vaccine Combination Was Superior in Real-world Study

After recognizing that the ChAdOx1 nCoV-19 (Oxford/AstraZeneca) vaccine caused rare but severe adverse reactions, European health authorities recommended that people younger than 55 years should switch to the BNT162b2 (Pfizer-BioNTech) vaccine for their second dose. A study published in Nature found the combination to be more effective and immunogenic than the standard BNT162b2 2-dose regimen.

The analysis of medical records from more than 13,000 health care workers in France revealed that, regardless of age, those who received 2 doses of the BNT162b2 vaccine were twice as likely to have a SARS-CoV-2 infection at least 2 weeks after full vaccination than those who received a ChAdOx1 nCoV-19 prime followed by a BNT162b2 boost.

To determine why, the researchers studied a group of health care workers’ anti-SARS-CoV-2 spike protein immune responses 4 weeks after receiving their second vaccine dose. Serum samples from those who received the mix-and-match regimen had greater neutralizing activity, including against the Delta variant and other variants of concern. However, workers who received the heterologous regimen were administered their second dose after a longer interval, a factor that could have improved their immune response.

Although confirmatory studies are needed, the findings suggest that the combination regimen could be particularly useful for immunocompromised patients, according to the authors.

Immunocompromised Patients With COVID-19 Receive Interferon Gamma

Clinicians reported in Med that 5 severely immunocompromised patients critically ill with COVID-19 received interferon gamma therapy as a last resort. All 5 individuals quickly cleared the virus after beginning the off-label treatment, and 4 recovered.

The patients had severe defects in their cellular immune responses, resulting in sustained high SARS-CoV-2 viral loads and loss of respiratory function requiring mechanical ventilation. They were unable to clear the virus over prolonged periods, despite repeated treatments with convalescent plasma or hyperimmune anti-COVID-19 intravenous immunoglobulin administration and remdesivir as an adjuvant.

The patients’ viral loads rapidly decreased and their respiratory function improved after the clinicians administered 100 mg of subcutaneous interferon gamma 3 times per week. The immunotherapy was well tolerated, with no signs of hyperinflammation based on plasma C-reactive protein, serum ferritin, and other indicators. One patient with severe intensive care unit–acquired weakness died after it was decided to withdraw mechanical ventilation.

Patients with pulmonary tuberculosis and pulmonary aspergillosis previously have been treated with interferon gamma, a cytokine with potent immunostimulatory effects. But according to the case study’s authors, its use in COVID-19 hasn’t appeared in the literature until now.

The treatments weren’t part of a randomized trial, so it can’t be said with certainty that they caused the patients’ viral clearance. The authors suggested that interferon gamma should be studied as an adjuvant therapy for severely immunocompromised patients whose persistently high SARS-CoV-2 loads aren’t clinically improving. They underscored that those with autoimmune or autoinflammatory disorders who receive the therapy for COVID-19 should be closely monitored for signs of hyperinflammation. – Jennifer Abbasi

Note: Source references are available through embedded hyperlinks in the article text online.