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Letter

SARS-CoV-2 vaccines for all but a single dose for COVID-19 survivors

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There is an urgent need to develop policies that maximize the number of people who receive vaccines without sacrificing the efficacy of immune protection given that we are still in the midst of the COVID-19 pandemic with a limited supply of authorized SARS-CoV-2 vaccines.

Several policy proposals have recently been discussed including delaying the second vaccine dose for everyone or focusing vaccinations in a preferred manner towards naïve individuals. We believe the best solution is to provide individuals who already had a SARS-CoV-2 infection receive only one (rather than two) shots of the currently authorized mRNA vaccines (BNT162b2/Pfizer; mRNA-1273/Moderna). Emerging real world evidence suggest that the antibody responses to the first vaccine dose in individuals with prior SARS-CoV-2 infection is equal to or exceeds the antibody titers found in naïve individuals after the second dose. Changing the current vaccine recommendation to provide only one dose of vaccine to COVID-19 survivors would free up many urgently needed vaccine doses. With the additional available vaccines, there would be no need to delay the second vaccine dose for naïve individuals.

Recent findings from several groups independently report high antibody titers and neutralization activity after the first dose of Pfizer or Moderna RNA vaccine in individuals who already had SARS-CoV-2 infections [1-5]. While each of these recent studies has a limited number of participants, the overall conclusions are complementary and clear with respect to the fact that individuals with pre-existing immunity developed uniformly high antibody titers. The observed increased reactogenicity experienced after the first dose in COVID-19 survivors [1,4] combined with rapid increase in antibody titers [1-5] supports the notion that the first vaccine dose acts as boost for the immune responses acquired after natural infection. In such a scenario, the second vaccine dose administered within 21-30 days after the first dose results in little increase in antibody titers [1,3]. It will be important to assess whether the same principles apply to vaccines developed on different platforms, with broad implications for global health.

Over 149 million people worldwide (32 million in the US) have been diagnosed with a SARS-CoV-2 infection since the beginning of the pandemic over a year ago with approximately 10% of the US population having had COVID-19 (Coronavirus COVID-19 Global Cases by Johns Hopkins CSSE, accessed 4/29/2021). Seroprevalence studies have shown pronounced geographic differences: for example in some of the US metropolitan centers that were hard hit during the first pandemic wave (e.g., NYC) around 20-25% of the inhabitants have antibodies to SARS-CoV-2. Thus, in some regions with a high percentage of confirmed previous infections, the mRNA vaccine supply could instantly increase without any significant increase in resources, freeing up doses to help contain the pandemic more swiftly, and potentially saving lives. Active antibody screening for SARS-CoV2 spike antibodies could further identify those with previous infection and increase the available supply even more.

Since the science shows that everyone benefits from the first dose of the mRNA vaccination, especially in the context of emerging variants of concern, COVID-19 survivors should not be deferred from

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vaccination. To the contrary, COVID-19 survivors should be offered a single dose, which would provide the needed immune boost to achieve high levels of immunity while limiting side effects and expanding the available vaccine supply to protect more individuals at risk in the immediate future. As vaccine supply chain limitations ease, booster vaccinations based on personalized schedules (informed by, for example, antibody titers) maybe required depending on the durability of the vaccine induced immune protection.

Contributors

This letter is the result of ongoing discussions between the authors. AH, FK, MS and VS wrote the initial draft. MF, AM, MR, RSH reviewed and edited the letter draft. All authors approved the final version. Each author generated original research on different aspects of the immune responses mounted in response to SARS-CoV2 vaccination as discussed in the letter.

Declaration of Competing Interest

Matthew Frieman, Anthony D. Harris, Ramin Sedaghat Herati, and Mohammad M. Sajadi have nothing to disclose. The Icahn School of Medicine at Mount Sinai has filed patent applications relating to SARS-CoV-2 95 serological assays and NDV-based SARS-CoV-2 vaccines which list Florian Krammer as co-inventor (US Provisional Application No 62/994,252). Viviana Simon is also listed on the serological assay patent application as co-inventor (US Provisional Application No 62/994,252). Mount Sinai has spun out a company, Kantaro, to market serological tests for SARS-CoV-2. Florian Krammer has consulted for Merck and Pfizer (before 2020), and is currently consulting for Seqirus and Avimex. The Krammer laboratory is also collaborating with Pfizer on animal models of SARS-CoV-2. Alberto Mantovani has consulted for Pfizer and Astra Zeneca. Maria Rescigno serves as a consultant for DiaSorin and Gelesis. Diasorin supports Humanitas for the development of diagnostic assays related to COVID-19 and has filed patent applications with Alberto Mantovani as co-inventor.

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