Impressive boosting of anti-S1/S2 IgG production in COVID-19-experienced patients after the first shot of the BNT162b2 mRNA COVID-19 Vaccine

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Dear Editor,

We read with interest the manuscript by Paul Bieniasz [1].

It is currently recommended that SARS-CoV-2 vaccines be administered regardless of exposure to SARS-CoV-2 infection [2], though little is known about differences in response magnitude and durability in COVID-19-naïve and COVID-19-experienced subjects. Our pilot study was aimed to describe anti-spike production after the first dose of the BNT162b2 mRNA COVID-19 Vaccine in COVID-19-naïve and COVID-19-experienced subjects, using the DiaSorin's LIAISON-CLIA-S1/S2® IgG solution, which has a 94.4% positive agreement to Plaque Reduction Neutralization Test (PRNT) [3].

After signing written informed consent subjects were enrolled in the AntiCROWN longitudinal study of anti-S1/S2 response, approved by the "Comitato Etico Interaziendale Area 1", n. 2020/ST/158. The pre-vaccine anti-S1/S2 levels for nursing home residents and staff (Elderly Nursing Home "San Giuseppe Moscati") were ascertained in June 2020 and subsequent SARS-CoV-2 exposure was monitored through nasopharyngeal swabs. Healthcare workers from the Luigi Sacco Hospital had anti-S1/S2 levels tested within 45 days before vaccination. Previous SARS-CoV-2 exposure was documented by a positive molecular swab or antigenic or serologic test. Participants were required to have a CLIA anti-S1/S2 test before and after the first vaccination.

Descriptive analyses of the variables were expressed as median (interquartile range [IQR]), or number (%). Continuous variables were compared using the nonparametric Mann-Whitney test. For the categorical variables the $\chi 2$ test was used, or Fisher's exact test when needed. The antibody levels before and after vaccination were compared between groups with Mann-Whitney test or Kruskal-Wallis with Dunn's test for pairwise multiple comparisons where appropriate.

We enrolled 52 COVID-19-naïve and 69 COVID-19-experienced subjects. Sixty-one were healthcare workers, 10 from the Luigi Sacco Hospital, and 51 from the nursing home (22 COVID-19-naïve) and 60 hosts (30 COVID-19-naïve). Populations were homogeneous by age and gender. Serology was assessed after a median of 9 days [IQR 7-11] after vaccination.

We didn't find significant differences in antibody responses by COVID-19 severity, as shown in Figure 1. In contrast, among COVID-19-naïve subjects the baseline antiS1/S2 IgG median value, 3.8 [IQR 3.8, 3.8] AU/mL remained quite the same, 3.70 [IQR 3.7, 4.9] AU/mL, while COVID-19-experienced levels increased from 53.0 [IQR 30.7, 93.6] AU/mL to 1800.0 [IQR 353.0, 3590.0] AU/mL ($p<0.001$). COVID-19-experienced serological non-responders didn't respond.

Such impressive and rapid boosting effect by the BNT162b2 mRNA COVID-19 Vaccine in COVID-19-experienced subjects confirms that their immunity has been primed by the viral infection itself and the first vaccination is a recall shot. Similar observations were posted in preprint manuscripts by Levi et al [4] on 124 healthcare workers, and by Kramer et al [5] in 41 SARS-CoV-2-exposed and 68 unexposed subjects and both concluded that in COVID-19-experienced subjects a second shot is probably not useful. Our cohort adds data on the comparable antibody production by elderly subjects.

Given such evidence it is reasonable to reorganize the vaccination campaign, assessing baseline immunity to SARS-CoV-2 through anti-S antibodies. At a time when vaccine demand outstrips supply, adopting this health strategy would help populations achieve herd immunity faster using fewer vaccine doses.

Notes

Potential conflicts of interest. None of the authors has potential conflicts of interest to disclose.

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Figure 1 Legend:

Anti-S1/S2 antibody, tested by DiaSorin's LIAISON-CLIA-Sa/S2® IgG before and after the first dose of the BNT162b2 mRNA COVID-19 vaccine, comparing COVID-19 naïve people vs. asymptomatic/Pauci-symptomatic COVID-19 people vs. symptomatic/hospitalized patients expressed (A) on a logarithmic scale (Log_{10}) and (B) as Arbitrary Units (AU/mL).

CN = COVID19 naïve people; A/P = asymptomatic/Pauci-symptomatic COVID-19 people; S/H = symptomatic/hospitalized patients

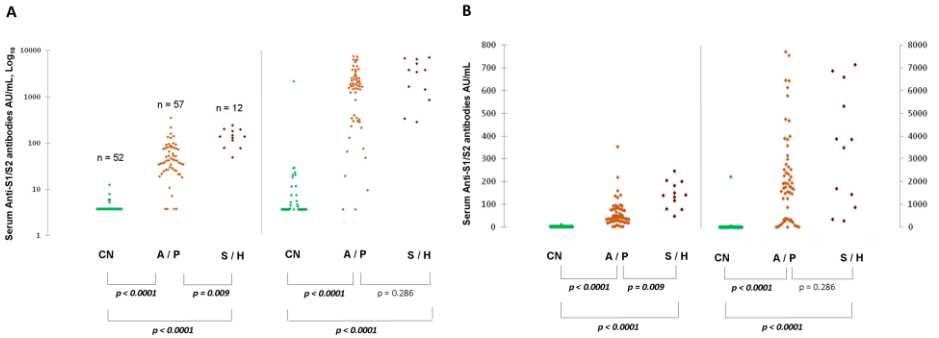

Fig. 1. Anti-S1/S2 antibody, tested by DiaSorin's LIAISON-CLIA-S1/S2® IgG before and after the first dose of the BNT162b2 mRNA COVID-19 Vaccine, comparing COVID-19 naïve people vs Asymptomatic/Pauci-symptomatic COVID-19 people vs Symptomatic/hospitalized patients expressed **(A)** on a logarithmic scale (Log_{10}), and **(B)** as Arbitrary Units (AU/mL).

CN = COVID-19 naïve people; A / P = Asymptomatic/Pauci-symptomatic COVID-19 people; S / H = Symptomatic/Hospitalized patients