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Anti-SARS-CoV-2 IgA Response in Baseline Seronegative and Seropositive Recipients of BNT162b2 mRNA COVID-19 Vaccine

To the Editor:

We read with interest the article by Iddins et al.,[1] reporting the immune response anti-SARS-CoV-2 IgG against the receptor binding domain (RBD) spike protein in healthcare workers. Since the risk of infection and poor outcomes seem also largely dependent on efficient anti-SARS-CoV-2 IgA response, assessing this antibody class is pivotal.[2]

Thus, we analyzed serum levels of total anti-spike RBD Ig, (Elecsys Anti-SARS-CoV-2S immunoassay on Roche Cobas 6000; Roche Diagnostics, Basel, Switzerland), anti-spike RBD IgG (ACCESS SARS-CoV-2 IgG II on Access 2; Beckman Coulter, Brea CA), and anti-spike S1 subunit IgA (Anti-SARS-CoV-2 ELISA IgA, manual ELISA; Euroimmun, Lübeck, Germany), in 24 healthcare workers undergoing vaccination with BNT162b2 mRNA COVID-19 at Peschiera del Garda hospital (Italy). This cohort comprised two matched samples of 12 baseline SARS-CoV-2 seronegative subjects (median age 40 years, interquartile range 31–52 years; 6 women) and 12 baseline SARS-CoV-2 seropositive subjects (median age 41 years, interquartile range 31–52 years; 6 women). Serum samples were drawn before the first vaccine dose, at 21 days (before the second vaccine dose) and 50 days afterwards. The study was conducted in accordance with the Helsinki Declaration and cleared by the Ethics Committee of Verona and Rovigo Provinces (3246CESC).

The results are summarized in Table 1. Levels of all antibodies increased in both baseline SASR-CoV-2 seronegative and seropositive cohorts, though such increase continued after the second dose in baseline seronegative subjects, while reached a plateau in baseline seropositive subjects. In agreement with earlier data published by Vicenti et al,[3] anti-SARS-CoV-2 RBD IgG levels after the first dose in baseline seropositive subjects were comparable to those achieved after two doses in baseline seronegative subjects (340.4 vs. 341.2 AU/mL; $P = 0.259$), while those of anti-SARS-CoV-2 RBD Total Ig (20,585.5 vs. 1629.0 AU/mL; $P < 0.001$) and anti-SARS-CoV-2 S1 Ig A (8.97 vs. 5.76 ratio; $P < 0.001$) were significantly higher. After the second dose, levels of anti-SARS-CoV-2 RBD Total Ig and Anti-SARS-CoV-2 S1 Ig A were still significantly higher in baseline seropositive subjects than in the seronegative cohort (both $P < 0.001$), while anti-SARS-CoV-2 RBD IgG levels were comparable ($P = 0.068$).

Our results, reporting anti-SARS-CoV-2 IgA antibodies response after BNT162b2 mRNA COVID-19 vaccination, suggest that consideration could be given to delay and/or omit the second vaccine dose in baseline SARS-CoV-2 seropositive subjects.

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TABLE 1. Serum Levels of anti-SARS-CoV-2 Antibodies (Median and Interquartile Range) in Baseline SARS-CoV-2 Seronegative and Seropositive Healthcare Workers, Undergoing BNT162b2 mRNA COVID-19 Vaccination

	Baseline			21 days			50 days		
Antibodies	**Seronegative**	**Seropositive**	***P****	**Seronegative**	**Seropositive**	***P****	**Seronegative**	**Seropositive**	***P****
Anti-SARS-CoV-2 RBD Total Ig (AU/mL)	0.4 (0.4–0.4)	92.5 (15.9–141.5)	<0.001	57.2 (21.2–98.0)	20,585.5 (11,902.0–24,527.5)	<0.001	1629.0 (1136.3–2587.0)	19,984.0 (14,394.8–25,000.0)	<0.001
Anti-SARS-CoV-2 RBD IgG (AU/mL)	0.2 (0.1–0.2)	10.0 (8.0–14.4)	<0.001	41.7 (23.1–88.1)	340.4 (241.8–433.2)	<0.001	341.2 (263.7–641.2)	306.4 (262.7–358.2)	0.068
Anti-SARS-CoV-2 S1 IgA (ratio)	0.23 (0.16–0.31)	1.17 (0.78–1.70)	<0.001	3.15 (2.02–5.65)	8.97 (8.79–10.41)	<0.001	5.76 (3.67–7.28)	8.76 (8.01–9.75)	<0.001

Ig, immunoglobulin; RBD, receptor binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
*Seropositive vs. seronegative.

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