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203.LYMPHOCYTES AND ACQUIRED OR CONGENITAL IMMUNODEFICIENCY DISORDERS

Kinetics of Anti-Sars-Cov-2 Antibody Responses 3 Months Post Complete Vaccination with BNT162b2; A Prospective Study in 283 Health Workers

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Abstract Background: Levels of neutralizing antibodies (NAbs) against SARS-CoV-2 correlate with clinically relevant immune protection from COVID-19. However, a slight decline in antibody titers has become evident even at one month following the second BNT162b2 shot, whereas increased time since the second vaccine dose has been associated with decreased NAb activity against SARS-CoV-2 variants. The aim of this study was to investigate the kinetics of NAbs and anti-S-RBD IgGs after vaccination of health workers with the BNT162b2 mRNA vaccine over a period of up to three months after the second shot. The possible influence of comorbidities, characteristics of the subjects, co-medication, and adverse events was also investigated.

Methods: All participants have been enrolled in a large prospective study (NCT04743388) evaluating the kinetics of anti-SARS-CoV-2 antibodies after COVID-19 vaccination. Main inclusion criteria for participation in this study were eligibility for vaccination according to the national program for COVID-19, age above 18 years, and ability to sign the informed consent form. Major exclusion criteria included the presence of active malignant disease, immunosuppressive therapy, and end-stage renal disease. According to National Immunization Program, access to the BNT162b2 mRNA vaccine was available to anyone 18 years of age or older.

NAbs and anti-S-RBD IgG titers were measured on days 1 (before the first vaccine shot), 8, 22 (before the second shot), 36, 50, and three months after the second vaccination (D111), using FDA approved methods, namely, cPass™ SARS-CoV2 NAbs Detection Kit (GenScript, Piscataway, NJ, USA) and Elecsys Anti-SARS-CoV-2 S assay (Roche Diagnostics GmbH, Mannheim, Germany), respectively.

Results: In total, 283 health workers (median age 48 years) were included in this study. On D1, immediately before vaccination, the median neutralizing inhibition was 14.2%, while 29 individuals (10.2%) had inhibition levels above the positive threshold of the method (30%). NAbs showed a rapid increase from D8 to D36 on a constant rate of about 3% per day and reached a median (SD) of 97.2% (4.7) at D36. From D36 to D50 a slight decrease in NAbs values was detected and it became more prominent between D50 and D111, when the rate of decline was determined at -0.11 per day. The median (SD) NAbs titers at D111 were 92.7% (11.8). Paired grouped comparisons using the Wilcoxon signed ranks test showed statistically significant differences in inhibition levels between pairs: D36 vs. D50, D36 vs. D111, and D50 vs. D111 (for all three comparisons p < 0.001) (Figure A).

A similar pattern was also observed for anti-S-RBD antibodies. It is worth mentioning that compared to NAbs, the maximum anti-S-RBD levels were reached two weeks later, i.e., at D36. Interestingly, anti-S-RBDs showed a steeper increase during D22-D36 and a lower decline rate during D36-D111. All consecutive pairs comparison, using Wilcoxon’s test, led to p-values < 0.001 (Figure B).

There was an almost linear relationship between NAbs and anti-S-RBD at D22 (Spearman’s rho correlation coefficient equal to 0.718). However, their relationship became non-linear from D36; this is due to the steep increase in anti-S-RBD levels that was observed during the D22-D36 period, while the corresponding increase rate for NAbs was much lower. Also, the decline of anti-S-RBD titers was lower compared to that of NAbs. The composite effect of these functions led to a non-linear pattern.

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Furthermore, prior COVID-19 and younger age were associated with superior antibody responses over time. Regarding those with previous positive PCR for SARS-CoV-2, significantly higher levels were observed at the initial phase (D1, D8) (Mann-Whitney p-values <0.001) and at D111 (p=0.046). From D50 there was a trend for a slower decline rate for those with previous positive PCR. Younger individuals had higher antibody titers at D36, D50, and D111, which is due to a slower decline in NAb levels compared to the older group of participants (for all three comparisons, Wilcoxon’s p-values were <0.05).

**Conclusions:** We found a persistent but declining anti-SARS-CoV-2 humoral immunity at 3 months following full vaccination with BNT162b2 in healthy individuals. Our longitudinal study is ongoing to determine the time point of NAb reduction below the positivity threshold; then a booster vaccine dose might be necessary to maintain humoral immunity against SARS-CoV-2.

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