Humoral and cellular response three months following bivalent booster administration

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Humoral and cellular response three months following bivalent booster administration

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INTRODUCTION

The development of COVID-19 vaccines permitted the reduction of SARS-CoV-2 infections, complications and death. A gradual decline in vaccine efficacy (VE) against infection over time has been observed within the first months after the initial two-dose regimen and soon after the administration of additional monovalent mRNA vaccine boosters. This waned efficacy was consistent with the decrease of neutralizing antibodies (NAbs) that represents the first line of anti-viral defense, supporting the role of NAbs as a strong correlate of COVID-19 protection. The aim of this study was to assess the humoral and cellular response in a cohort of heathcare workers that received either the BA.1 or the BA.4/5 bivalent booster.

METHOD

Population:

- **58 healthcare workers**.
- Blood collection: **0 – 14 – 28 – 90 days** after administration.
- 50 participants received bivalent BNT162b2 booster (**BA.1**), 8 received bivalent BNT162b2 booster (**BA.4/5**).

In this cohort we assessed:

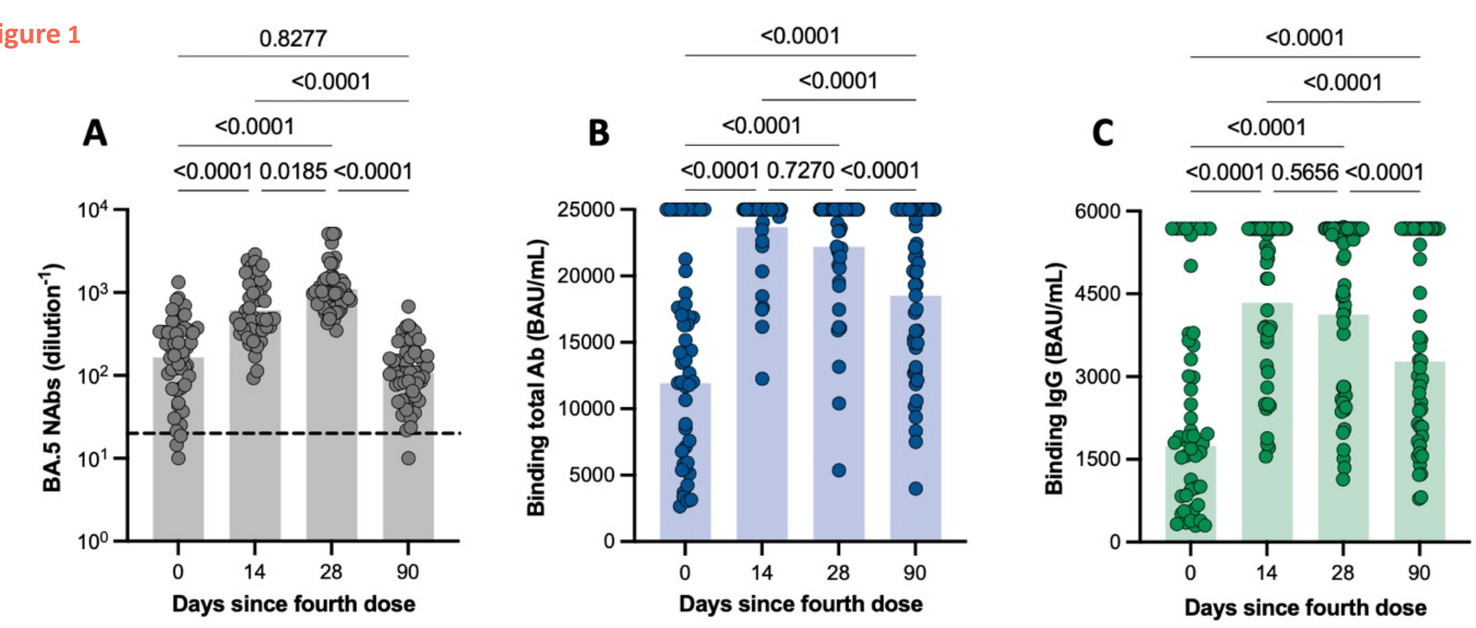
- Humoral response, using **neutralizing antibodies** against the BA.5 Omicron variant, and **binding total and IgG antibodies**.
- The cellular response, by means of **interferon gamma** (IFNγ) that was released from T cells in response to an *in vitro* SARS-CoV-2 stimulation.

Statistical analysis:

- Median and interquartile range (IQR) were used to present demographic data and geometric mean titers (GMT) and 95% confidence intervals (95% CI) to present the results of the humoral and cellular response
- A Mann-Withney test was used to assess potential difference between the type of adapted booster (BA.1 versus BA.4/5) and between participants that had a history of past infection or not.

RESULTS

Figure 1



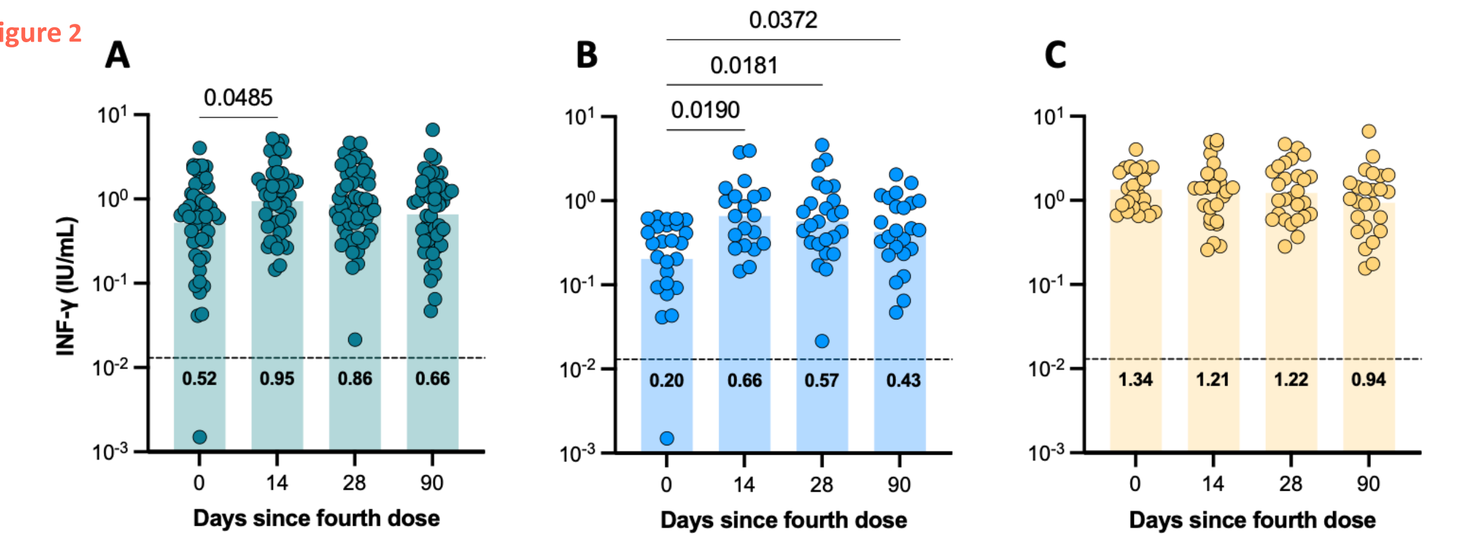
- The highest measured neutralizing capacity against the BA.5 variant was reached at **day 28 with a GMT of 1,098** (95% CI = 920–1,310), representing **a significant 6.7-fold increase** from baseline (i.e., 165; 95% CI = 120–227, p < 0.0001). **A significant decrease was then observed at 90 days** with an observed **GMT of 107** (95% CI = 85.7–136, p < 0.0001), which represents a **10.3-fold decrease**.

- The proportion of detectable neutralizing antibodies (i.e., <1:20) was 94.8%, 100%, 100%, and 98.3% at baseline, 14, 28, and 90 days. (**Figure 1A**) According to the kinetic model, **a mean time of 135 days** (95% CI = 72–170) in would be needed **to cross the dilution titer threshold of 1/20** (NAbs positivity threshold).

- Considering the binding antibodies, the highest measured titers of both binding IgG and total antibodies was reached at **day 14 with a GMT of 4,340** (95% CI = 3,892–4,838) and **of 23,682** (95% CI = 22,755–24,646), corresponding to **a 2.5-fold and 2.0-fold increase** from baseline, respectively (p < 0.0001). Between 14 and 90 days, **a significant 1.3-fold decrease** was observed for both binding IgG and total antibodies (p < 0.0001). (**Figure 1B, 1C**)

- For neutralizing antibodies, binding antibodies and binding IgG, the kinetics was **not significantly different if considering the BA.1 booster and the BA.4/5 booster** separately (p > 0.05).

Figure 2



- All participants except one had detectable levels of IFNγ at baseline. At **14 days, a significant 1.8-fold increase** was observed (0.52 versus 0.95 IU/mL, p = 0.0485). After 28 and 90 days, the levels of IFNγ that **slowly decreased at 0.86 and 0.66 IU/mL failed to reach the significance level** (p > 0.05). (**Figure 2A**)

- If we focus the analysis on the participants that had **lower levels of IFNγ** before the booster administration (i.e., < median of 0.65 IU/mL), **the fold-increase at 14 days was higher** (i.e., 3.3) and levels of IFNγ at 28 (0.57 IU/mL) and 90 days (0.43 IU/mL) were also significantly higher compared to baseline (0.20 IU/mL, p < 0.05) (**Figure 2B**).

- In participants presenting **higher IFNγ levels** at baseline (i.e., > median of 0.65 IU/mL), **no significant difference were observed afterward**, even if a slight decrease was observed. As for the humoral response, **participants that received the BA.4/5 booster did not present higher levels of IFNγ compared to the ones that received BA.1 booster** (p = 0.7821) (**Figure 2C**).

CONCLUSION

The increase of neutralizing antibodies following the administration of bivalent BA.1 or BA.4/5 boosters that we documented in our study (i.e., 6.7-fold increase) **was consistent with the conclusions of other studies** (i.e., 4.5 to 17.4-fold increase). The two studies of Wang *et al.* and Collier *et al.* found that boosting with the new bivalent mRNA vaccine targeting both the BA.4/5 variant and the D614G strain did not elicit a superior neutralizing capacity after 1 month against the D614G strain and Omicron subvariants (including BA.4/5, BA.4.6 and BA.2.75), as compared with boosting with the original monovalent vaccine. **Although most participants still had a robust cellular response before the bivalent booster administration**, an increase in the cellular response by means of IFNγ assessment was observed after 2 weeks, especially in participants that had lower levels of IFNγ just before the booster administration. **The monitoring of the humoral and cellular response could be useful to identify patients with a poor adapted immunity that would need to benefit first from an additional booster.**

CONTACT INFORMATION

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