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CORRESPONDENCE

# Induction of High Neutralizing Activity Against Both Omicron BA.2 and Omicron BA.1 by Coronavirus Disease 2019 Messenger RNA Booster Vaccination

To the Editor—Assawakosri et al [1] reported that heterologous booster vaccines significantly increased binding and neutralizing antibodies (nAbs) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern (VOCs), including the Omicron variant (BA.1) in individuals immunized with 2 doses of CoronaVac, indicating possible vaccine strategies to thwart VOCs. The most recently designated VOC of SARS-CoV-2, Omicron, is associated with an increased risk of reinfection [2]. Among 4 sublineages of Omicron (BA.1, BA.1.1, BA.2, and BA.3), BA.1 has spread to >151 countries and is responsible for the greatly increased number of coronavirus disease 2019 (COVID-19) cases worldwide. However, Omicron BA.2 has also been detected in ≥85 countries and became the dominant lineage in 18 countries by mid-February 2022 [3]. BA.2 has become the next dominant variant worldwide.

A recent epidemiological study in South Africa suggested that the clinical profile of illness caused by BA.1 infection is similar to that caused by BA.2 [4]. Although BA.2 infection has generally been associated with mild illness, its high transmissibility may be accompanied by high numbers of cases with considerable societal impacts (eg, greater work absences).

In response to the surge in Omicron BA.1 cases, booster vaccination was initiated in many countries. In addition to the study reported by Assawakosri et al [1], our study and others showed that BA.1 escapes 2 doses of BNT162b2 messenger RNA vaccine-induced neutralization and that a booster (third) vaccination is required to induce the nAb against BA.1 [5, 6].

There is, however, limited evidence regarding the effectiveness of a booster vaccination against BA.2 [7, 8]. Therefore, we collected blood samples from 84 physicians at Kobe University Hospital in Kobe, Japan, in January 2022 (median age, 44 years; interquartile range, 33–58 years) about 7 months after they had received 2 BNT162b2 vaccinations and about 2 weeks after their first booster vaccination. We performed a serum neutralizing assay against BA.2 using authentic virus, as described elsewhere [5]. No participants had a history of SARS-CoV-2 infection. The study was approved by the ethical committee of the Kobe University Graduate School of Medicine (approval code B200200). All participants were recruited and provided written informed consent.

The results demonstrated that, similar to results with BA.1 [5], most participants had no or a very low nAb titer against BA.2 at 7 months after 2 BNT162b2 vaccinations (geometric mean titer, 1.18 [95% confidence interval 1.09–1.27]). However, the titer increased significantly 2 weeks after the booster vaccination (geometric mean titer, 36.44 [95% confidence interval, 30.53–43.50]; $P < .001$) (Figure 1).

These results indicate that a booster vaccination could induce neutralizing immunity against Omicron BA.2 (as it has against BA.1) and that a booster dose of BNT162b2 messenger RNA vaccine induces a high cross-neutralizing response against SARS-CoV-2 variants [5]. This may indicate that booster

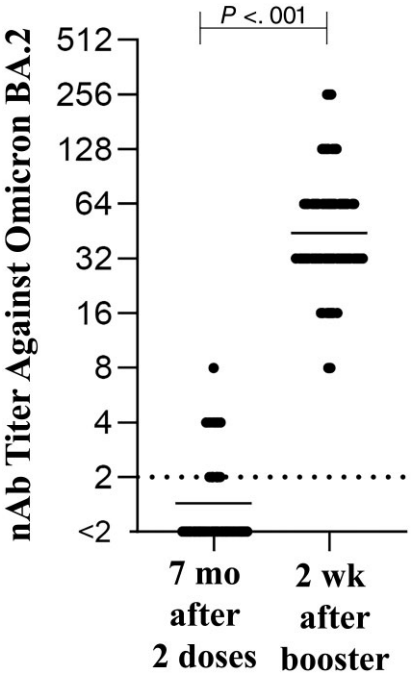


**Figure 1.** Neutralizing antibody (nAb) titers against Omicron BA.2 in BNT162b2 messenger RNA–vaccinated men (n = 84) at 7 months after they had received 2 vaccine doses and at 2 weeks after a booster vaccination. Dotted horizontal line represents the limit of detection; solid horizontal lines, the geometric mean titers. Titers were compared by means of the 2-sample Wilcoxon rank sum (Mann-Whitney) test; 2-tailed *P* values were calculated.

vaccination is a meaningful approach for the suppression of BA.2 pandemic and can activate memory B cells that produce nAbs recognizing epitopes conserved among SARS-CoV-2 variants.

## Notes

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