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LETTER TO THE EDITOR

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Neutralizing potency of COVID-19 vaccines against the SARS-CoV-2 Omicron (B.1.1.529) variant

To the Editor,

The recent emergence of a new variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) called Omicron (B.1.1.529) has raised paramount concerns in scientific and medical communities due to the presence of several mutations in the spike protein, many of which are located within the receptor-binding domain (RBD).[1] Some of these mutations were found to have a substantial influence on host cells receptors and anti-SARS-CoV-2 antibodies binding,[2] which may then impact infectivity and neutralizing antibodies escape, thus potentially magnifying the risk of coronavirus disease 2019 (COVID-19) vaccine breakthrough. We have hence carried out a scientific literature search, aimed at summarizing the currently published evidence on Omicron variant neutralizing properties of serum or plasma collected from recipients of COVID-19 vaccines.

We carried out an electronic search in Medline and Scopus, using the keywords "vaccine" AND "Omicron" OR "B.1.1.529" AND "SARS-CoV-2" AND "neutralization" OR "antibodies," with no language or date limits (i.e., up to January 2, 2022). Title, summary, and (eventually) full text of all documents identified based on these search criteria were scrutinized, and those reporting complete information on the neutralization properties of COVID-19 vaccines against the SARS-CoV-2 Omicron (B.1.1.529) variant, with or without the adjunctive effects of booster vaccine doses administrated after completing a primary vaccination cycle, were included in our analysis. Due to the wide heterogeneity and scarce comparability of commercial immunoassays for measuring anti-SARS-CoV-2 antibodies, only studies using live or pseudotyped virus neutralization assays were retained. The reference list of all documents was also analyzed for identifying other potentially eligible investigations. The following data were retrieved from all included studies: type of vaccine(s) used for primary vaccination, type of assay used for studying serum or plasma neutralizing properties, decreased neutralization of Omicron (B.1.1.529) variant compared to an ancestral strain, and/or the currently endemic Delta variant, type of vaccine used for administering the booster dose and, finally, increased level of Omicron (B.1.1.529) neutralization achieved after administering the booster dose.

Overall, 52 items could be originally detected based on our search criteria, and seven more could be identified from the reference lists, thus leading to 59 potentially eligible studies. Nonetheless, 45 of such documents ought to be omitted since they did not fulfill our aforementioned search criteria. Our final analysis could thus only include 14 published studies (Table 1),[3–16] which used the following vaccines: Pfizer/BioNTech BNT162b2 in 10 studies, Moderna mRNA-1273 in three studies, AstraZeneca ChAdOx1, Johnson & Johnson Ad26.COV2.S, Sinovac CoronaVac, and Sinopharm BBIBP-CorV in two studies, while Novavax NVX-CoV2373 and Sputnik V vaccines were only used in one study, respectively. Live and pseudotyped virus neutralization assays were used in four and nine studies, respectively, while the remaining study used a hACE2 (angiotensin-converting enzyme 2) receptor-binding test. Ten out of these 14 studies described also the neutralizing activity achieved after administering vaccine booster doses (Table 1).

In all included studies, a decreased neutralization of SARS-CoV-2 Omicron B.1.1.529 variant was evidenced in postvaccination samples, ranging between −4.3-folds to the absence of neutralization compared to an ancestral SARS-CoV-2 strain, and between −2.1-folds to the absence of neutralization compared to the Delta SARS-CoV-2 variant, respectively (Table 1). For vaccines used in ≥3 studies, decreased neutralization of SARS-CoV-2 Omicron B.1.1.529 compared to an ancestral strain was comprised between 15- and 127-folds in Pfizer/BioNTech BNT162b2 recipients, between 9- and 122-folds in those receiving Moderna mRNA-1273, and between 12- and 20-folds in those receiving Sinopharm BBIBP-CorV, respectively. In all studies, the COVID-19 vaccine booster doses were effective to elicit a sustained enhancement of SARS-CoV-2 Omicron B.1.1.529 neutralization, with such increase being comprised between 3- and 133-folds compared to the pre-booster period (Table 1).

The results of this preliminary analysis of currently available research reveal that the neutralizing potency of all COVID-19 vaccines seems to be reduced against the newly emerged SARS-CoV-2 Omicron (B.1.1.529), though the administration of vaccine booster doses is seemingly effective in substantially restoring post-immunization efficacy against this new and highly mutated lineage. This is not really unpredictable, as over 30 mutations characterizing this new variant are located within the spike protein (15 within its RBD), and this would hence predispose this new lineage to escape therapies based on monoclonal antibodies as well as vaccine-elicited antibodies (2). Vaccine boosters seem hence strongly advisable for limiting the risk of SARS-CoV-2 Omicron (B.1.1.529) breakthrough infections by enhancing anti-SARS-CoV-2 antibodies titers, especially in fragile populations or in those at higher risk of infection (e.g., immunocompromised patients).

CONFLICT OF INTERESTS

The author declares that there are no conflict of interests.

TABLE 1 Neutralizing potency of coronavirus disease 2019 (COVID-19) vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron (B.1.1.529) variant

	Primary vaccination			Booster vaccine dose	
Authors	**Vaccines; sample collection**	**Neutralization assay**	**Reduced Omicron neutralization (folds)**	**Vaccines; sample collection**	**Increased Omicron neutralization after booster (folds) compared to pre-booster**
Dejnirattisai W et al. (2021)[3]	2 × ChAdOx1 or 2 × BNT162b2; ~28 days	Live virus neutralization assay	Vs. ancestral strain: ChAdOx1: ↓ × 13.3; BNT162b2: ↓ × 29.8 Vs. delta variant: ChAdOx1: ↓ × 5.2; BNT162b2: ↓ × 25.1	No	-
Ai J et al. (2021)[4]	2 × BBIBP-CorV; ~14 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: BBIBP-CorV: ↓ × 11.6; Vs. delta variant: BBIBP-CorV: ↓ × 7.9	1 × BBIBP-CorV; 14–28 days	BBIBP-CorV: ↑ × 9.6
Garcia-Beltran WF et al. (2021)[5]	2 × BNT162b2 or 2 × mRNA-1273; <3 months	Pseudotyped virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 43; mRNA-1273: ↓ × 122	1 × BNT162b2 or 1 × mRNA-1273; <3 months	BNT162b2 ↑ × 27; mRNA-1273: ↑ × 19
Doria-Rose NA et al. (2021)[6]	2 × mRNA-1273; ~14 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: mRNA-1273: ↓ × 8.9	1 × mRNA-1273; 14 days	mRNA-1273: ↑ × 12.6
Schmidt F et al. (2021)[7]	2 × BNT162b2 or 1 × Ad26.COV2.S; ~1.3 month	Pseudotyped virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 127; Ad26.COV2.S: No neutralization	1 × BNT162b2 or 1 × Ad26.COV2.S; ~30 days	BNT162b2: ↑ × 42.1; Ad26.COV2.S: unavailable
Cameroni E et al. (2021)[8]	2 × BNT162b2 or 2 × mRNA-1273 or 2 × ChAdOx1 or 1 × Ad26.COV2.S; 2 × Sinovac; 2 × Sptunik; 14–28 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 44; mRNA-1273: ↓ × 33; ChAdOx1: ↓× 36; Ad26.COV2.S: No neutralization; Sinovac: No neutralization; Sptunik: No neutralization	No	-
Lu L et al. (2021)[9]	2 × BNT162b2 or 2 × Sinovac; ~1 month	Live virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 38.7; Sinovac ↓ × 4.3 Vs. delta variant: BNT162b2: ↓ × 21.0; Sinovac ↓ × 2.1	No	-
Cele S et al. (2021)[10]	2 × BNT162b2; 10–63 days	Live virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 22	No	-
Muik A et al. (2021)[11]	2 × BNT162b2; ~21 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 22.8 Vs. delta variant: BNT162b2: ↓ × 10.4	1 × BNT162b2; ~28 days	BNT162b2: ↑ × 23.4
Mallory R et al. (2021)[12]	2 × NVX-CoV2373; ~14 days	hACE2 receptor-binding test	Vs. ancestral strain: NVX-CoV2373: ↓ × 8.2 Vs. delta variant: NVX-CoV2373: ↓ × 2.8	1 × NVX-CoV2373; ~28 days	NVX-CoV2373: ↑ × 14.8
Yu X et al. (2021)[13]	2 × BBIBP-CorV; ~28 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: BBIBP-CorV: ↓ × 20.1	1 × BBIBP-CorV; ~28 days	BBIBP-CorV: ↑ × 3.3

TABLE 1 (Continued)

Authors	Primary vaccination			Booster vaccine dose	
	Vaccines; sample collection	Neutralization assay	Reduced Omicron neutralization (folds)	Vaccines; sample collection	Increased Omicron neutralization after booster (folds) compared to pre-booster
Haveri A et al. (2021)[14]	2 × BNT162b2; ~21 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 19.7	1 × BNT162b2; ~28 days	BNT162b2: ↑ × 38.4
Gruell H et al. (2021)[15]	2 × BNT162b2; ~28 days	Pseudotyped virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 68.2 Vs. delta variant: BNT162b2: ↓ × 21.5	1 × BNT162b2; ~21 days	BNT162b2: ↑ × 132.8
Nemet I et al. (2021)[16]	2 × BNT162b2; ~166 days	Live virus neutralization assay	Vs. ancestral strain: BNT162b2: ↓ × 14.9 Vs. delta variant: BNT162b2: ↓ × 7.2	1 × BNT162b2; ~25 days	BNT162b2: ↑ × 96.9

Note: AstraZeneca ChAdOx1 (adenovirus-based); Johnson & Johnson Ad26.COV2.S (adenovirus-based); Moderna mRNA-1273 (mRNA-based); Novavax NVX-CoV2373 (recombinant spike protein vaccine); Pfizer/BioNTech BNT162b2 (mRNA-based); Sinopharm BBIBP-CorV (inactivated); Sinovac CoronaVac (inactivated); Sputnik V vaccine (adenovirus-based).

DATA AVAILABILITY STATEMENT

Data available on request.

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