

Neutralization of Omicron Subvariants BA.5 and BQ.1 After Four COVID-19 Vaccine Doses in PLWH Receiving ART

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Background

- Limited data exist regarding the humoral immune benefits of fourth COVID-19 vaccine doses in people living with HIV (PLWH) who are receiving suppressive antiretroviral therapy (ART).
- As most PLWH have now experienced COVID-19, it is also important to assess the benefits of fourth doses in this context.

Study Objective

In 2021 we established a prospective, longitudinal observational study in context of Canada's mass COVID-19 vaccine rollout to evaluate the strength and durability of vaccine immune responses in PLWH.

- Here, we quantify wild-type and Omicron-specific live virus neutralization in 63 COVID-19-naïve and -experienced PLWH following four doses of COVID-19 vaccine.**

Methods

- Plasma was collected one month after fourth vaccine doses in **63 PLWH**.
- Wild-type (WT)-, Omicron-BA.5- and Omicron-BQ.1-specific neutralization activities were quantified using a live virus assay.
- Multiple linear regression was used to investigate the relationship between sociodemographic, health and vaccine-related variables and SARS-CoV-2 neutralization following four-dose vaccination.

Table 1: Study Population

Characteristic	PLWH (n=63)
HIV-related variables	
Receiving antiretroviral therapy, n (%)	63 (100)
Most recent plasma viral load, copies HIV RNA/mL, median [IQR]	<50 [<50 - <50]
Most recent CD4+ T-cell count in cells/mm3, median [IQR]	720 [540 - 920]
Nadir CD4+ T-cell count in cells/mm3, median [IQR]	280 [90 - 530]
Sociodemographic and health variables	
Age in years, median [IQR]	57 [44 - 65]
Female sex at birth, n (%)	9 (14)
White ethnicity, n (%)	46 (73)
Number of chronic conditions, median [IQR]	1 [0 - 1]
SARS-CoV-2 infection history, n (%)	
Naïve	19 (30%)
Infection - pre-Omicron era	12 (19%)
Infection - Omicron era	32 (51%)
Vaccine details	
Initial two-dose regimen, n (%)	
mRNA-mRNA	51 (81)
ChAdOx1 - mRNA (heterologous)	6 (9.5)
ChAdOx1 - ChAdOx1	6 (9.5)
Days between first and second doses, median [IQR]	59 [53 - 67]
Third dose, n (%)	
BNT162b2	21 (33)
mRNA-1273	42 (67)
Days between second and third doses, median [IQR]	182 [134 - 192]
Fourth dose, n (%)	
BNT162b2 monovalent	9 (14%)
BNT162b2 bivalent	9 (14%)
mRNA-1273 monovalent	19 (30%)
mRNA-1273 bivalent	26 (41%)
Days between third and fourth doses, median [IQR]	258 [217-282]

Conclusions

- Fourth COVID-19 vaccine doses provide immunologic benefits to all PLWH on ART regardless of SARS-CoV-2 infection history.
- COVID-19-experienced PLWH showed significantly higher neutralization post-fourth dose compared to COVID-19-naïve PLWH, consistent with humoral benefits of 'hybrid' immunity.
- COVID-19-experienced PLWH displayed comparable Omicron-BA.5 and BQ.1-specific neutralization regardless of the pandemic era of their SARS-CoV-2 infection (pre-Omicron vs. Omicron eras).
- Omicron-BA.5-specific neutralization was significantly lower than WT in all PLWH regardless of COVID-19 experience. Omicron-BQ.1-specific neutralization was significantly lower still.
- Bivalent vaccines that incorporate Omicron BA.1 or BA.4/BA.5 immunogens did not appear to elicit superior neutralization compared to the original monovalent vaccines.
- These results support current public health recommendations that all adults receive a fourth COVID-19 vaccine dose within 6 months of their third vaccine dose (or their most recent SARS-CoV-2 infection).

Acknowledgements

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Fig. 1: Fourth doses enhance neutralization against WT and BA.5 regardless of prior infection

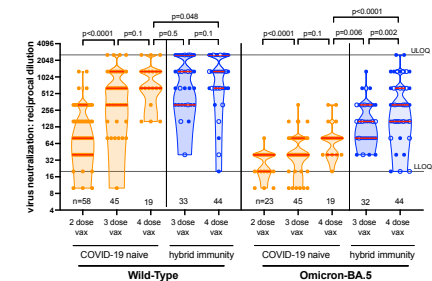
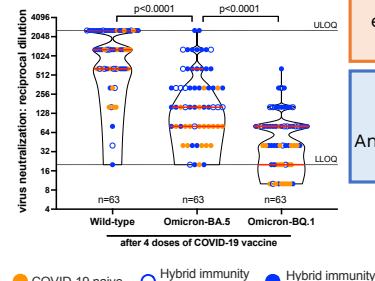


Fig. 2: Nevertheless, Omicron-BA.5 and BQ.1-specific neutralization remain markedly lower than WT



Multivariable analyses: Bivalent responses comparable to monovalent

Bivalent fourth doses did not further enhance neutralization to WT, BA.5 nor BQ.1 compared to monovalent

Strongest correlate of WT neutralization
An mRNA-1273 fourth dose (regardless of valency)

Strongest correlate of both BA.5 and BQ.1 neutralization
Prior COVID-19, regardless of pandemic era

Fig. 3: Neutralization is higher in COVID-19-experienced vs. -naïve PLWH

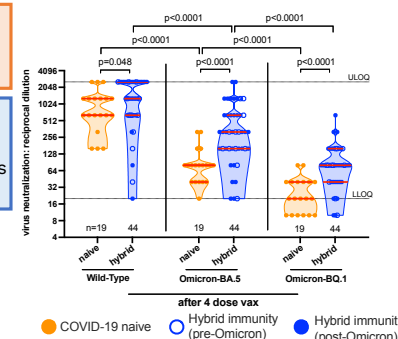


Fig. 4: Among COVID-19-experienced PLWH, infection era does not influence Omicron neutralization

