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

Hope R. Lapointe[1], Peter K. Cheung[1,2], Yurou Sang[2], Siobhan Ennis[2], Francis Mwimanzi[2], Sarah Speckmaier[1], Evan Barad[1,2], Winnie Dong[1], Janet Simons[3,4], Christopher F. Lowe[3,4,5], Marc G. Romney[3,4,5], Chanson J. Brumme[1,6], Masahiro Niikura[2], Mark A. Brockman[1,2,7], Zabrina L. Brumme[1,2] and the COVID-19 vaccine immunity study team

[1] British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada; [2] Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada; [3] Department of Pathology and Laboratory Medicine, Providence Health Care, Vancouver, Canada; [4] Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada; [5] Division of Medical Microbiology and Virology, St. Paul's Hospital, Vancouver, Canada; [6] Department of Medicine, University of British Columbia, Vancouver, Canada; [7] Department of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, Canada;

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 (%)	
Naive	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-specfic 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

We thank the participants, without whom this study would not have been possible.

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

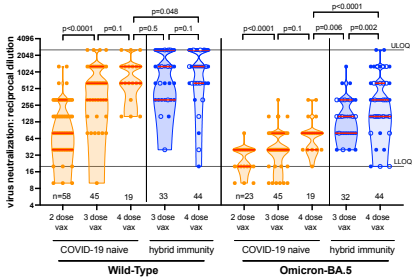
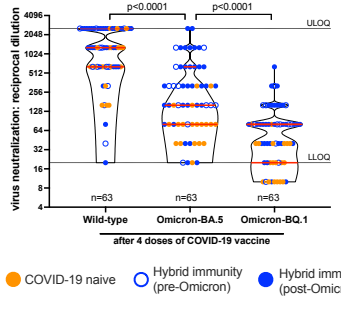


Fig. 2: Nevertheless, Omicron-BA.5 and BQ.1-specific neutralization remain markedly lower than WT



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

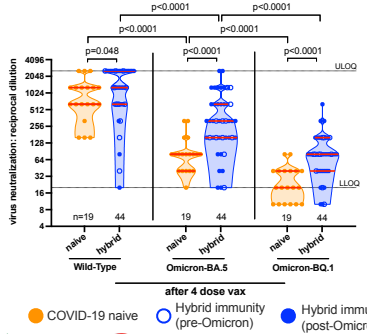
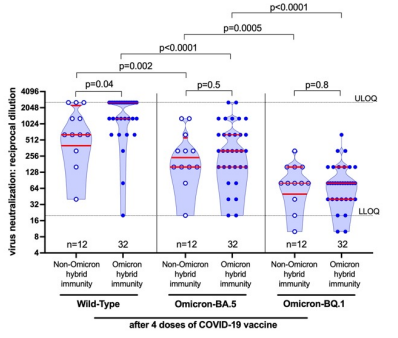


Fig. 4: Among COVID-19-experienced PLWH, infection era does not influence Omicron neutralization



The COVID-19 vaccine immunity study team comprises: Aslam Anis, Rolando Barrios, Laura Burns, Curtis Cooper, Cecilia T. Costiniuk, Sneha Datwani, Mari L. DeMarco, Maggie C. Duncan, Bruce Ganase, Silvia Guillemi, Marianne Harris, Malcolm Hedgcock, Daniel Holmes, Mark Hull, Rebecca Kalikawe, Victor Leung, Julio S.G. Montaner, Nadia Moran-Garcia, F. Harrison Omondi, Natalie Prystajecky, Paul Sereda, Junine Toy, Gisele Umviligihozo, Fatima Yaseen, and Landon Young.