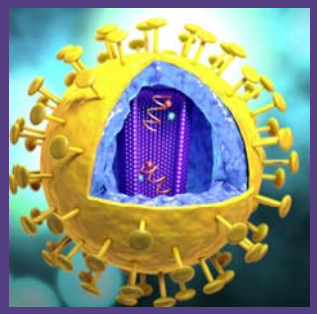
Viral Blip post-ChAdOx1 nCoV-19 (AZD1222) Vaccine In A Patient With Controlled HIV



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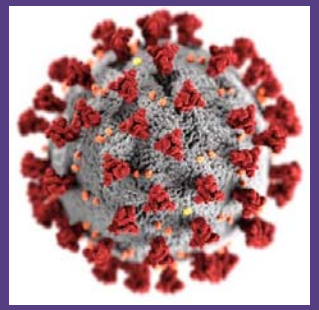

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Background

- COVID-19 has caused unprecedented morbidity and mortality
  - >400 million infections and ~6 million deaths as of April, 2022 [1]
- Persons living with HIV (PLWH) have been disproportionately affected…
  - …as per a recent meta-analysis involving 22 global studies showing PLWH had both increased COVID-19 infection rates and mortality, compared to those without HIV [2]
- Fortunately, rapid COVID-19 vaccine developments have resulted in…
  - …improved COVID-19 disease immunity amidst largely tolerable adverse events

Viral Blips

- *Viral blips*: an increase in HIV viral load from undetectable to 50-500 copies/mL [3], though this definition is variable
- 2007-2013: Swedish HIV cohort found viral blips were observed in 10% of patients [3]
- 2000: PLWH on ART (viral load (VL) < 50 copies/mL) were administered the influenza vaccine and…
  - Found to have a transient increase in HIV viral load two weeks post-vaccine [4]
  - Authors attributed this increase in viral load to the mobilization of a reservoir of latently-infected CD4 cells [4]

[1] Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*; published online Feb 19. https://doi.org/10.1016/S1473-3099(20)30120-1. https://coronavirus.jhu.edu/map.html Accessed April 8, 2022.
[2] Ssentongo P, Heilbrunn ES, Ssentongo AE, Advani S, Chinchilli VM, Nunez JJ, Du P. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. *Sci Rep*. 2021 Mar 18;11(1):6283.
[3] Sörstedt E, Nilsson S, Blaxhult A, *et al*. Viral blips during suppressive antiretroviral treatment are associated with high baseline HIV-1 RNA levels. *BMC Infect Dis*. 2016;16:305. Published 2016 Jun 21.
[4] Günthard HF, Wong JK, Spina CA, Ignacio C, Kwok S, Christopherson C, Hwang J, Haubrich R, Havlir D, Richman DD. Effect of influenza vaccination on viral replication and immune response in persons infected with human immunodeficiency virus receiving potent antiretroviral therapy. *J Infect Dis*. 2000 Feb;181(2):522-31.

COVID Vaccines in PLWH

- ChAdOx1 nCoV-19 (*AstraZeneca®*) vaccine was evaluated in 54 PLWH in a single-arm open label sub-study in London, UK [5]
  - Patients received combination anti-retroviral therapy (cART) and had undetectable HIV RNA levels or viral load (< 50 copies/mL), with an average CD4 cell count of 694 cells/uL
  - PLWH had a similar immune response to those without HIV, and experienced mild adverse events. Viral loads were not reported post-vaccination.

- BNT162b2 mRNA COVID-19 (*Pfizer®*) vaccine was studied in 143 PLWH in Israel [6]
  - Patients received cART and 95% had an undetectable viral load, with an average CD4 cell count of 700 cells/uL
  - Similar to the ChAdOx1 nCoV-19 vaccine in PLWH study above, this vaccine produced an immune response in PLWH similar to those without HIV, with minimal adverse events
  - CD4 cell counts were found to be significantly decreased after first and second doses of BNT162b2 vaccines (2-3 weeks after each vaccine), and viral loads increased in three patients (after the second vaccine dose) from undetectable to 47, 52, and 92 copies/mL.

[5] Frater J, *et al.*, Oxford COVID Vaccine Trial Group. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial. *Lancet HIV.* 2021 Jun 18;8(8):e474–85.
[6] Levy I, Wieder-Finesod A, Litchevsky V, Biber A, Indenbaum V, Olmer L, Huppert A, Mor O, Goldstein M, Levin EG, Hod T, Cohen C, Lustig Y, Rahav G. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in people living with HIV-1. *Clin Microbiol Infect.* 2021 Aug 24:S1198-743X(21)00423-7.

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Case Report: Viral Blip post-ChAdOx1 nCoV-19 Vaccine

- Male; 65-70 years; living in Ontario, Canada
- HIV+; dx in 2003; CD4 cell count nadir of 230 cells/uL and baseline VL = 23,625 copies/mL
- ARVs initiated at time of diagnosis
  - VL generally undetectable throughout treatment history (viral blip in 2014 = 78 copies/mL while on TDF/FTC/RPV)
- Past ARV history (chronologically): NVP+AZT/3TC, EFV+AZT/3TC, TDF/FTC + ATV/r, TDF/FTC/RPV, TAF/FTC/RPV, DTG/3TC
- Concurrent meds: ramipril, hydrochlorothiazide, valacyclovir

Date	Lab/Intervention	Comments
Feb 2020	CD4 = 391 (%), VL = undetectable	TAF/FTC/RPV (started 2019)
Jan 2021	VL = undetectable	TAF/FTC/RPV
Mar 31, 2021	ChAdOx1 nCoV-19 (*AstraZeneca*®) administered	TAF/FTC/RPV mild injection site pain and one day of fatigue
May 28, 2021	VL = 422 copies/mL Genotyping = no mutations Viral blip 8 weeks post-AZ vaccine	TAF/FTC/RPV patient reported perfect ARV compliance with no acute infections or medication changes
Jun 7, 2021	VL = 102 copies/mL	TAF/FTC/RPV
Jun 17, 2021	VL = undetectable	TAF/FTC/RPV
Jun 22, 2021	BNT162b2 mRNA COVID-19 (*Pfizer*®) administered	TAF/FTC/RPV no adverse events noted by patient
Jun 25, 2021		Patient requested a change from TAF/FTC/RPV to DTG/FTC
Jun 29, 2021	VL = undetectable	DTG/FTC
Jul 28, 2021	VL = undetectable	DTG/FTC
Dec 9, 2021	VL = undetectable	DTG/FTC

Discussion

- Vaccine administrations have been associated with viral blips; this COVID-19 HIV case is unique because:

1. Timing of viral blip was eight weeks post-vaccination
    - Viral blips were seen two weeks post-influenza vaccines [4], and 2-3 weeks post-BNT162b2 mRNA vaccine [6]; thus, viral blip may have been higher if it had been measured 2-3 weeks post-ChAdOx1 nCoV-19 vaccine
2. Viral blip was not observed both 1 and 5 weeks post-BNT162b2 mRNA vaccine
    - In the Israeli study [6], patients experienced viral blips 2-3 weeks post-second COVID vaccination
3. Practice of mixing COVID-19 vaccines is novel
    - This case may provide safety data and considerations for PLWH receiving mixed vaccines
    - This knowledge combined with mixed vaccine efficacy data (i.e. antibody response measurements), could impact vaccine allocation strategies, mixing and matching vaccines, side effect profiling, etc., particularly with the arrival of booster shots

Conclusion

- COVID-19 vaccines remain the most widely accepted method to end the coronavirus pandemic
    - PLWH on ART may experience a viral blip as long as two months post-vaccination; **additional precautions should be recommended to ensure that the HIV virus is not transmitted during viral blips**