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# HIV-1 DNA Testing in Viremic Patients Demonstrates a Greater Ability to **Detect Drug Resistance Compared to Plasma Virus Testing**

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#### I. Background

- Treatment guidelines recommend drug resistance testing on plasma virus to guide the selection of antiretroviral therapy in patients with HIV-1 viremia >500 copies/mL<sup>1</sup>
- Drug resistance mutations (DRMs) in plasma virus represent only the selective pressure imposed by the failing regimen and may miss DRMs reflective of prior regimens. DRMs also may be lost from plasma virus in prolonged absence of antiretroviral therapy (ART)<sup>2-4</sup>
- HIV-1 DNA testing derives resistance information from peripheral blood mononuclear cells (PBMCs) and offers a resistance testing option when plasma virus is undetectable. HIV-1 DNA testing may also capture DRMs in virus that is actively replicating in viremic patients, but such use of the assay has not been characterized

### II. Methods

- HIV-1 RNA derived from plasma and HIV-1 DNA derived from PBMCs were obtained from the same patient on the same day for 89 patients with viral loads >500 copies/mL
- Drug resistance testing on plasma virus was performed using PhenoSense GT Plus Integrase®, and on HIV-1 DNA using GenoSure Archive® (Monogram Biosciences)
- DRM and antiretroviral susceptibility concordance was assessed between the genotypic results of PhenoSense GT Plus Integrase® and GenoSure Archive® for 103 paired tests
- "Resistance" and "resistance possible" assessments on test reports were scored as drug resistance The impact of viral load on result concordance was assessed using Spearman's correlation and Mann-Whitney U test

### III. Results

Table 1. Patient and virus characteristics.		Table 2. Drug resistance characteristics.		
Characteristic	n (% or range)	Characteristic	Plasma virus	PB
Female Pregnant	78 (88%) 15 (19%)	Resistance reported, n NRTI NNRTI PI INSTI 1-class 2-class 3-class 4 class	(HIV-1 RNA)	(HI
Mean age, years <30 30-40 40-50 50-60 >60	38 (19-71) 25 36 32 9 2		77 110 27 24 42	98 123 50 26 39
HIV-1 subtype B	82 (92.1%)		8 0	13 7 1
AG C A1 G	4 (4.5%) 1 (1.1%) 1 (1.1%) 1 (1.1%)	DRMs detected, n 548 633 c/mL, copies per milliliter; DRM, drug resistance mutation; integrase inhibitor; NRTI, nucleos(t)ide reverse transcripta NNRTI, non-nucleoside reverse transcriptase inhibitor; PB peripheral blood mononuclear cell; PI, protease inhibitor; N		
Mean VL at resistance testing, c/mL	132,487 (780 - 2,980,000)			







ance mutation; INSTI rse transcriptase inhibitor:

ease inhibitor; VL, viral load.

**IV. Summary and Conclusion** 

- HIV-1 DNA testing largely captured drug resistance detected in contemporaneous plasma virus, with greatest concordance in patients with viral loads >10,000 c/mL, and identified additional drug resistance mutations in 49% of cases
- In this analysis, among patients with viral loads greater than 500 copies/mL, HIV-1 DNA testing identified DRMs and resistance more often than HIV-1 plasma virus testing

## V. References and Acknowledgements

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• The percentage of PBMC compartment DRMs that were detected in plasma virus did not correlate with viral load at time of resistance testing (Spearman's rho = 0.052; p = 0.60) • No significant difference was observed in the percentage of PBMC compartment DRMs that were

detected in plasma virus in samples from patients with viral loads >10,000 c/mL or <10,000 c/mL



- Among 89 patients with 103 paired plasma-PBMC HIV-1 drug resistance tests:
  - More DRMs were found in the PMBC compartment in 49% (50/103) of test pairs
  - More DRMs were found in plasma virus in 10% (10/103) of test pairs
- 92% (505/548) of plasma virus DRMs were also detected in the PBMC compartment, while 80%
- (505/633) of DRMs found in the PBMC compartment were also detected in plasma virus (Figure 1A)
- 89% (211/238) of antiretroviral resistance calls made for plasma virus were also made for virus in the PBMC compartment, while 71% (211/297) of resistance calls made for virus in the PBMC compartment
- Across all drug classes, PBMC compartment testing identified more DRMs and more antiretroviral resistance calls than plasma virus testing (Figure 2) to nearly all antiretrovirals (Figure 4)
- M184V was identified in 24 patients, and was captured 79% of the time using PBMC compartment
- PBMC compartment testing of HIV-1 DNA captured a greater percentage of plasma virus DRMs in patients with viral loads >10,000 c/mL than in those with viral loads <10,000 c/mL (Figure 5A) • PBMC compartment DRMs were detected in a manner independent of viral load at time of resistance

**1.** Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed 05/28/2020. **2.** Devereux, Helen L., et al. AIDS 13.18 (1999): 123-127. **3.** Deeks, Steven G., et al. NEJM 344.7 (2001): 472-480. **4.** Castro, Hannah, et al. "Persistence of HIV-1 transmitted drug resistance mutations." JID 208.9