

Setting the Stage for Transmission of Drug resistance: Genital HIV Shedding and Drug Resistance in Men and Women.

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I. Background and Objectives

- Background.** Virologic failure, and viremia occurs in 20-50% of ART recipients and is associated with selection of
- Drug resistance and genital tract shedding of HIV-1.**

Objectives:

- (1) To determine class and drug specific resistance (genotype) of plasma virus associated with genital tract virus shedding.
- (2) To compare the selection of drug resistance and the frequency of genital tract shedding among men and women on ART.

II. Study Design

- A5077 is a multicenter, cross-sectional and longitudinal study of HIV-1 viremia and genital tract shedding. Here we examined differences in baseline viral load, (plasma) virus genotype and genital virus among men and women with viremia.
- Analysis focused on 29 subjects on ART within 10 days of sampling and 53 subjects on ART within 90 days of study entry.
- The primary comparison was between viremic men and women, recently exposed to ART with plasma HIV-1 RNA > 2,000 c/mL

III. Methods

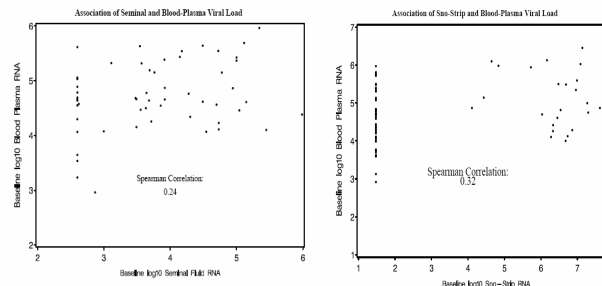
- Genital specimens matched with blood plasma: Semen (64); CxVag fluid (80);
- Complete history of ART.
- Laboratory: HIV-1 genital and plasma RNA measured using RT-PCR (Roche), NASBA (Organon), real-time RT-PCR RT-PCR Sequencing of RNA extracts:
Plasma Genotyping: Labs
 TrueGene Vanderbilt, UNC
 Stanford ABI Stanford
 In House validated Seattle

Methods (2) – subsets of those receiving ART at sampling

Men and Women with matched genital tract samples.
 Identify, drug class specific plasma resistance using HIVDB.stanford.edu (HIVSeq).
 Genotypic susceptibility score (GSS), for individual regimens.
 N=53, 23 men and 30 women, on drug within 90 days,
 N=29, 13 men and 16 women on drug within 10 days.

Characteristic at entry	All n=144	ART < 90 days n=53	ART < 10 days n=29
Age, median (range) years	41 (36-45)	43 (39-46)	42 (39-46)
Number of previous ARV median (IRQ)	5 (0.5-7.5)	7(4-9)	8 (5-10)
Years since first ART median (IQR) years	1.4 (0-3.2)	5.8 (3.8-8.5)	6.8 (4.8-10.4)
CD4 cell count / mL, median (IRQ)	235 (90-305)	263 (105-332)	210 (110-306)
Plasma HIV-1 RNA, median log ₁₀ c/mL (IQR)	4.8 (4.3-5.4)	4.6 (4.1-5.1)	4.6 (4.1-4.8)

IV. Results (1) Genital shedding in Men and Women



Results (2) Gender, resistance, and genital shedding

Gender comparison of Genotypic resistance, mean (SD) number of resistant ARV classes among 50 subjects on drug within 90 days

	Men (23)	vs	Women (30)
NRTIs	2.57 (2.96)		1.86 (2.60)
PIs	2.05 (3.04)		1.45 (2.75)
NNRTI	0.90 (1.34)		1.62 (1.42)

men trended towards less NNRTI resistance
 More PI resistance, (Wilcoxon rank-sum test, P=0.08)
 > 50% of the women had resistance to >2 NNRTI drugs.

Genotypic susceptibility score (GSS) Genital HIV shedding among those on ART within 10 days

GSS ≤2 Men 5/9 vs. Women 1/10
 GSS > 2 Men 3/3 vs. Women 0/5,
 (M:8/12 vs W:1/15, RR 9.8 [95%CI, 2.2,171])

with those not on ARVs
 (M:41/51 vs W:28/64, RR 1.8 [1.4,2.6])

suggests a greater impact of continued therapy on the genital viral load of women (P=0.03).

V. Summary and Conclusions

- Among these highly drug experienced patients, failing ART, most had resistance to at least 2 classes of ARVs, with trends towards differences between men and women in the selection of class specific resistance.

- Overall, the frequency of genital tract HIV shedding was ~ 2-fold greater among men.

- However, among those receiving ART at the time of sampling, genital shedding was markedly higher among men compared to women, which persisted after controlling for plasma HIV RNA (P<0.001).

- Genital shedding of virus in the setting of continued ART and high levels of genotypic drug resistance is more common (~ 10 fold) among men compared to women.

- These observations may, in part explain the increasing frequency of drug resistance among newly infected men who have sex with men and suggest that there a lower risk of the transmission of drug resistance from women to men through heterosexual contact.