



# Enhanced Survival Associated with use of HIV Susceptibility Testing among HAART-Experienced Patients in the HIV Outpatient Study (HOPS)

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## ABSTRACT

**Background and Objective:** HIV genotype and phenotypic susceptibility testing (G/PT) use optimizes antiretroviral (ARV) drug selection, HIV suppression and CD4 cell responses in ARV-experienced patients. We evaluated the impact of G/PT use on survival rates in a large cohort of HAART-treated patients followed multiple years.

**Methods:** We analyzed data from HAART-experienced participants in the HOPS, a multi-center, prospective, observational study of U.S. HIV-infected persons. We included 4,186 HAART-experienced patients, seen from 1/1/99-6/30/05, whose plasma HIV RNA measurements after starting their first HAART regimen revealed >1000 copies/cc, and who were followed a median of 4.14 years (interquartile range:2.06-6.63). We used logistic regression analysis to examine predictors of G/PT. We used Cox proportional hazards (PH) models to compare survival rates among those who did vs. did not undergo G/PT. We adjusted for significant baseline demographics (age, HIV risk factor), baseline and nadir CD4 cell counts (CD4), and insurance status.

**Results:** 1,056 (25% of the total) HAART-experienced patients underwent G/PT, of whom 613 were triple-ARV-class experienced (TCE), 3,130 HAART-experienced did not undergo G/PT. The median number of HAART regimens before the first G/PT was 3. In a Cox PH analysis that adjusted for baseline CD4, ARV status (HAART vs. no HAART), age at first VL test (> or ≤ 40 years), date of first G/PT, insurance type (public vs private), and HIV risk (IDU vs. non-IDU), those having had ≥1 G/PT had a 59% improvement in survival (HR=0.41, p<0.01) (Figures 1 and 2). The strongest predictor of survival was baseline CD4 (Figures 1 and 2). Among TCE, comparison of 151 patients who died to 151 survivors, matched on the factors adjusted for in the Cox PH model, showed improved survival associated with having had ≥ 1G/PT (HR=0.31, p<0.001) (Table 2).

**Conclusions:** In the HOPS, the use of HIV susceptibility testing was strongly associated with improved survival after adjusting for stage of HIV disease, demographics, age, and calendar time (year). Presumably, this survival benefit reflects long-term improvements in HIV suppression and CD4 counts achievable with G/PT-guided HAART selection. However, G/PT use may also reflect improvements in other aspects of care.

### The Cohort

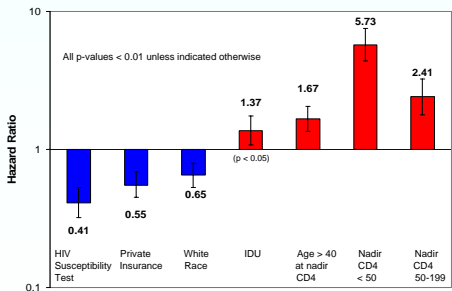
•1,263 patients who underwent HIV susceptibility testing (1,056 HAART-exp., 207 AR-naïve), and who were under observation since 1999.

•3,351 patients who did not undergo HIV susceptibility testing (3,130 HAART-exp., 221 AR-naïve), and who were under observation since 1999.

Independent binary variables for analysis:

- Race/ethnicity (white, non-white)
- AR-naïve
- Gender
- Intravenous drug use
- Insurance type (private, public)
- Age at CD4+ nadir (>40, <40)

Figure 1: Cox proportional hazards analysis of independent variables and outcome of death among entire cohort (N=4614)



Red background: HR > 1 and statistically significant, Blue background: HR < 1 and statistically significant

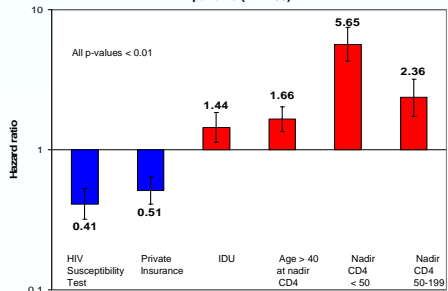
• Figure 1: Cox PH analysis revealed that enhanced survival was associated with having undergone HIV susceptibility testing, having private insurance, and being white. Reduced survival was associated with having a history of injection drug use, age>40 years, and nadir CD4>50 or 51-199.

Table 1: Cohort Characteristics

	HIV Susceptibility Test		p-value
	Yes (%) (N=1263)	No (%) (N=3351)	
Male gender	1029 (81%)	2677 (80%)	0.243
White race	775 (61%)	1945 (58%)	0.044
Age > 40 yrs.	555 (44%)	1616 (48%)	0.010
Private Insurance	761 (60%)	1864 (56%)	0.005
Median CD4 (Q1, Q3)	170 (55, 320)	226 (76, 383)	<.001
Median log viral load (Q1, Q3)	4.4 (3.3, 5.0)	3.9 (1.5, 4.8)	<.001

•Table 1: Those most likely to undergo HIV susceptibility testing were white, less than 40 years of age, had private insurance, lower CD4 cell counts, and higher HIV viral load levels

Figure 2: Cox proportional hazards analysis of independent variables and outcome of death among HAART-experienced patients (N=4186)



• Figure 2: Cox PH analysis among HAART-experienced patients revealed that enhanced survival was associated with having undergone HIV susceptibility testing and having private insurance. Reduced survival was associated with having a history of injection drug use, age>40 years, and nadir CD4>50 or 51-199.

Table 2: Mortality reduction associated with the use of HIV susceptibility tests— Cox proportional hazards analysis

Population	HIV Susceptibility Test		Hazard Ratio <sub>adj.</sub>	Confidence Interval	p-value
	Yes (N=151)	No (N=151)			
Case-matched, viremic and triple-class ART treated*	12/151 (7.9%) 32.9 per 1000 person-years**	33/151 (21.8%) 76.6 per 1000 person-years	0.31	0.16-0.60	<.001

\* Matched on year of CD4+ nadir, CD4+ nadir range, private insurance (y/n), IDU (y/n)

\*\* Since start of triple-class experience

• Table 2. Among triple class HAART-experienced patients who were persistently viremic, comparison of 151 patients who died to 151 survivors, matched on factors significant in the Cox PH model, revealed enhanced survival associated with having undergone ≥ 1 HIV susceptibility test.

## Conclusions

1. Those most likely to have undergone HIV susceptibility testing had lower CD4 cell counts, higher plasma HIV RNA levels, were white, had private insurance, and were less than 40 years of age.
2. Use of HIV susceptibility testing in the HOPS was strongly associated with enhanced survival (approx. two-fold death risk reduction, HR= 0.41) even after adjusting for stage of HIV disease, demographics, age and calendar time (year).
3. Among those who were triple ART class experienced yet persistently viremic, use of HIV susceptibility testing was associated with a three-fold reduction in death risk (HR=0.31).
4. Presumably these survival benefits reflect long-term improvements in HIV suppression and CD4 counts that are achievable with the use HIV susceptibility testing-guided HAART selection.

