
**Antiretroviral use and Misuse in the
Dominican Republic:
Implications for HIV Drug Resistance**

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CUMC and HIV in the DR.

- Karen Brudney, Director of the HIV clinic, received an NIH Fogarty research training grant in 2003 implemented through two NGOs, El Instituto Dermatológico y Cirugia de Piel, Profamilia.
- Over HIV 300 patients are on antiretroviral treatment and 800 followed between the two clinics.

**INSTITUTO
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En este centro se ofrecen los siguientes servicios:

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HIV in the Dominican Republic

- Population 9 million
- Prevalence of HIV estimated between 1.3 and 2.7%

HIV situation in the Dominican Republic

- Approximately 180,000 people infected.
- Global Fund For AIDS, TB and Malaria approved in 2003 but disbursement delayed until spring 2005 due to failures to implement basic changes needed to develop a national HIV program.
- Approximately 2000 total people on antiretroviral treatment today.

Factors contributing to HIV epidemic.

- Mainly Heterosexual transmission
- Thriving Sex tourism industry
- Poor, loosely regulated health care system.
- Significant Haitian Immigrant population who are systematically excluded from the health care systems.

Factors concerning for HIV drug resistance

- Private Doctors and clinics selling medications to patients.
- GNI per capita: US\$2,080 (World Bank, 2005)
- Most private doctors are untrained in HIV treatment and care.

Factors concerning for HIV drug resistance

- Medication transfers from Abroad, principally from the United States.
- Little support for patient education and adherence built into national treatment program.
- Single Dose Nevirapine for pMTCT

Health care demand by type of provider, 1996 (utilization as % of total seeking care; rows add to 100)

Indicator	SESPAS	IDSS	Private	Self-medication ^a	Other ^b
Rural					
Outpatient visits	29	<1	20	43	7
Hospital admissions	57	2	38	–	3
Urban					
Outpatient visits	22	2	28	42	6
Hospital admissions	43	4	48	–	4
Poorest 20%					
Outpatient visits	31	3	16	45	5
Hospital admissions	62	6	30	–	2
Richest 20%					
Outpatient visits	15	3	36	41	5
Hospital admissions	29	3	64	–	4
National					
Outpatient visits	25	2	25	42	6
Hospital admissions	49	3	44	–	4

Source: Macro International [1].

^a Purchase of medicines without physician visit.

^b Includes military and NGO providers, and traditional healers.

“Pharmacies are omnipresent in all urban areas, and general stores located in peripheral barrios and rural towns are generally well stocked with pharmaceutical products demanded by the population.”

G. La Forgia *et al.* Fend for yourself: Systemic failure in the Dominican health system . *Health Policy* 67 (2004) 173–186

Amplification of HIV drug resistance

- The WHO recommended standardized HIV treatment regimens are based on medications that have a low genetic barrier to resistance.

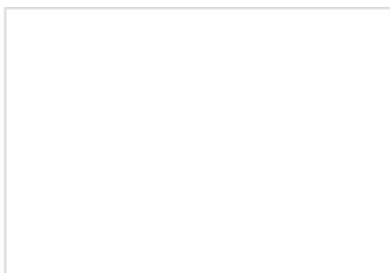
NRTI	NRTI	NNRTI
Zidovudine or Stavudine	<i>Lamivudine</i>	<i>Nevirapine</i> <i>or Efavirenz</i>

GeneSeq™

HIV DRUG RESISTANCE ASSAY



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Patient Name	DOB	Patient ID	Gender	ViroLogic Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status
Referring Physician				Reference Lab ID
Comments	HIV-1 Subtype [§] : B			

	Drug	GENESEQ™	ASSESSMENT*	Comments	
NRTI	Generic Name	Brand Name	Drug Resistance Associated Mutations Detected	Drug	
	Abacavir	Ziagen	M41L, D67N, K70R, M184V, K219K/Q	ABC Reduced Susc.	
	Didanosine	Videx	M41L, D67N, M184V, K219K/Q	ddl Sensitive	
	Emtricitabine	Emtriva	M41L, D67N, K70R, M184V, K219K/Q	FTC Reduced Susc.	
	Lamivudine	EpiVir	M41L, D67N, K70R, M184V, K219K/Q	3TC Reduced Susc.	
	Stavudine	Zerit	M41L, D67N, K70R, K219K/Q	d4T Sensitive	
	Tenofovir	Viread	M41L, D67N, K70R, K219K/Q	TFV Reduced Susc.	
	Zidovudine	Retrovir	M41L, D67N, K70R, K219K/Q	ZDV Reduced Susc.	
	NNRTI	Delavirdine	Rescriptor	None	DLV Sensitive
		Efavirenz	Sustiva	None	EFV Sensitive
Nevirapine		Viramune	None	NVP Sensitive	
PI	Atazanavir	Reyataz	L10I, I54L, L63P	ATV Sensitive	
	Fosamprenavir	Lexiva	L10I, V32V/I, I47V, I54L, L63P	AMP Reduced Susc.	
	Indinavir	Crixivan	L10I, V32V/I, I54L, L63P	IDV Sensitive	
		Crixivan / r99	L10I, V32V/I, I47V, I54L, L63P	IDVr Sensitive	
	Lopinavir	Kaletra	L10I, V32V/I, I47V, I54L, L63P	LPV/r Sensitive	
	Nelfinavir	Viracept	L10I, I54L, L63P	NFV Sensitive	
	Ritonavir	Norvir	L10I, V32V/I, I54L, L63P	RTV Sensitive	
	Saquinavir	Fortovase	L10I, I54L, L63P	SQV Sensitive	

§ For more information about HIV-1 subtype, please visit www.ViroLogicHIV.com.

* Assessment of drug susceptibility is based upon detected mutations and interpreted using an advanced proprietary algorithm (version 3).

† Interpretation algorithm derived from studies using IDV 800mg + RTV 200mg Q12h.

SUMMARY OF MUTATIONS OBSERVED

RT M41L, D67N, K70R, R83K, Q102K, K122E, C162S, D177E, I178L, M184V, G196G/E, R211K, K219K/Q, V241W/L, V245E, A272P, R277K, T285A
 PI L10I, I13V, V32V/I, R41K, I47V, I54L, D60E, L63P, I64V, H69Y

This test meets the standards for performance characteristics and all other quality control and assurance requirements established by the Clinical Laboratory Improvement Act. GeneSeq™ HIV is a DNA sequence assay based on primer extension and chain termination that analyzes the protease (amino acids 1-99) and reverse transcriptase (amino acids 1-355) coding regions in HIV-1. GeneSeq™ HIV is validated for testing specimens with HIV-1 viral loads equal to or above 500 copies/mL and should be interpreted only on such specimens. The results should not be used as the sole criteria for patient management. These results have been disclosed to you from confidential records protected by law and are not to be disclosed to unauthorized persons. Further disclosure of these results is prohibited without specific consent of the persons to whom it pertains, or as permitted by law.

Our Pilot Plan

- Administer a detailed questionnaire regarding previous ARV treatment history.
- Genotype and Phenotype resistance testing of all patients with detectable viral loads, including for patients who are treatment naïve.

Our Pilot Plan

- Multivariate logistic regression analysis will have viral resistance (yes, no) as the outcome variable and controlling for prior treatment, adherence, number of medicines administered per treatment, type of treatment (e.g. medicines sent from abroad, self administered treatment, etc.), payment for medications, and various demographic variables.