PhenoSENSE GT™ REPLICATION CAPACITY
COMBINATION HIV DRUG RESISTANCE ASSAY

Monogram BIOSCIENCES
LabCorp Specialty Testing Group

Samuel H. Pepkowitz, MD, Medical Director
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Patient Name:	DOB	Patient ID/Medical Record #	Gender	Monogram Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status
			Reference Lab ID/Order #	
Comments			HIV-1 Subtype: B	

	DRUG			PHENOSENSE™ SUSCEPTIBILITY			Evidence of Susceptibility		Net Assessment	
	Generic Name	Brand Name	Cutoffs (Lower - Upper)	Fold Change	Increasing Drug Susceptibility Decreasing (.1 / 1 / 10 / 100)		Pheno Sense	Gene Seq		
NRTI	**Abacavir**	Ziagen	***(4.5 - 6.5)***	**3.98**			**Y**	**N**	**Sensitive**	16
	Didanosine	Videx	***(1.3 - 2.2)***	**1.99**			**P**	**N**	**Partially Sensitive**	
	Emtricitabine	Emtriva	*(3.5)*	**>MAX**			**N**	**N**	**Resistant**	
	Lamivudine	Epivir	***(3.5)***	**>MAX**			**N**	**N**	**Resistant**	
	Stavudine	Zerit	***(1.7)***	**1.51**			**Y**	**N**	**Sensitive**	3
	Zidovudine	Retrovir	*(1.9)*	**7.91**			**N**	**N**	**Resistant**	3
	Tenofovir	Viread	***(1.4 - 4)***	**1.16**			**Y**	**N**	**Sensitive**	3
	NRTI Mutations		**M41L, M184V, T215Y**							
NNRTI	**Delavirdine**	Rescriptor	*(6.2)*	**3.91**			**Y**	**N**	**Sensitive**	1
	Efavirenz	Sustiva	*(3)*	**30**			**N**	**N**	**Resistant**	
	Etravirine	Intelence	***(2.9 - 10)***	**0.56**			**Y**	**N**	**Sensitive**	1
	Nevirapine	Viramune	*(4.5)*	**>MAX**			**N**	**N**	**Resistant**	
	Rilpivirine	Edurant	*(2)*	**1.29**			**Y**	**N**	**Resistant**	1
	NNRTI Mutations		**Y188Y/F/L, H221H/Y**							
PI	**Atazanavir**	Reyataz	*(2.2)*	**4.96**			**N**	**N**	**Resistant**	
		Reyataz / r‡	***(5.2)***	**4.96**			**Y**	**N**	**Sensitive**	16
	Darunavir	Prezista / r‡	***(10 - 90)***	**1.34**			**Y**	**Y**	**Sensitive**	
	Fosamprenavir	Lexiva / r‡	***(4 - 11)***	**4.00**			**Y**	**Y**	**Sensitive**	
	Indinavir	Crixivan / r‡	***(10)***	**5.81**			**Y**	**Y**	**Sensitive**	
	Lopinavir	Kaletra‡	***(9 - 55)***	**1.69**			**Y**	**Y**	**Sensitive**	
	Nelfinavir	Viracept	*(3.6)*	**17**			**N**	**N**	**Resistant**	
	Ritonavir	Norvir	*(2.5)*	**4.30**			**N**	**N**	**Resistant**	
	Saquinavir	Invirase / r‡	***(2.3 - 12)***	**3.88**			**P**	**N**	**Partially Sensitive**	
	Tipranavir	Aptivus / r‡	***(2 - 8)***	**2.87**			**P**	**N**	**Partially Sensitive**	
	PI Mutations		**L10V, I13V, K20T, E35G, M36I, I62V, L63T, T74S, L90M**							

Lower Clinical Cutoff (in bold)
Upper Clinical Cutoff (in bold)
Biological Cutoff
Hypersusceptibility Cutoff
Sensitive
Partially Sensitive
Resistant
Y Evidence of Drug Sensitivity
P Evidence of Partial Drug Sensitivity
N Evidence of Drug Resistance

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Patient Name:	Date Collected:	Monogram Acc#:	Status:

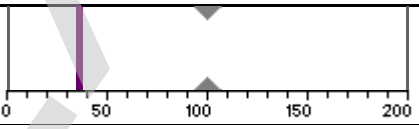
Combination Phenotype/Genotype Net Assessment

	SENSITIVE	PARTIALLY SENSITIVE	RESISTANT
NRTI	**Abacavir** **Stavudine** **Tenofovir**	**Didanosine**	**Emtricitabine** **Lamivudine** **Zidovudine**
NNRTI	**Delavirdine** **Etravirine**		**Efavirenz** **Nevirapine** **Rilpivirine**
PI	**Atazanavir / r** **Darunavir / r** **Fosamprenavir / r** **Indinavir / r** **Lopinavir / r**	**Saquinavir / r** **Tipranavir / r**	**Atazanavir** **Nelfinavir** **Ritonavir**

RC

Virus Replication Capacity = 36%

(Range 23%-57%)



Replication Capacity (RC) indicates the ability of the virus to replicate in the absence of drug. Range represents 95% confidence interval around RC measurement. 100%=median RC of wild-type viruses.

Phenotype / Genotype Comments (clinical significance may vary)

1 - **Mixture**: Mixtures detected at resistance-associated position(s); minor populations with decreased susceptibility may be present and may increase in the presence of drug pressure.
3 - **IC50 reduced**: Phenotypic measurement reflects possible enhanced susceptibility due to M184I or V.
16 - **Unexplained discordance**: Genotypic correlates of susceptibility not accounted for by current rules.

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Complete List of Mutations Detected

RT: P19P/L, V21V/I, V35V/I, M41L, V60I, Q102K, K122K/E, I135T, C162S, M184V, Y188Y/F/L, G196E, Q207E, T215Y, H221H/Y, A272A/S, R277R/K, L283I, P294T, E297E/K

PR: L10V, I13V, K14K/R, I15V, K20T, E35G, M36I, N37D/E, I62V, L63T, I64V, E65D, I72V, T74S, V77I, L90M, I93L

Important Definitions

IC50: Concentration of drug required to inhibit viral replication by 50%.

Fold Change = $\frac{\text{IC50 patient}}{\text{IC50 reference}}$

Clinical Cutoffs: *Lower clinical* cutoff denotes the fold change which was the best discriminator of reduced clinical response using drug- specific clinical outcome data. Reduced response was defined by the clinical endpoint for the specific clinical cohort analyzed for each cutoff value. *Upper clinical cutoff* denotes the fold change above which a clinical response is unlikely (<.5 log reduction in HIV RNA) and which was determined using the same drug-specific clinical cohort data as for the lower clinical cutoff. Biological cutoffs are used for specific antiretrovirals (ZDV, the NNRTIs and specific protease inhibitors when not pharmacokinetically enhanced with ritonavir). These values are defined as the fold change value below which reside 99% of tested wild-type isolates, i.e., those without known drug resistance mutations. Fold Change <0.4 indicates enhanced susceptibility.

Mixtures are indicated by amino acids separated by a slash. Deletions in the amino acid sequence are indicated by a ^ symbol.

ǂ **Boosted PIs:** Clinical cutoff and genotypic interpretation algorithms for ritonavir-boosted protease inhibitors derived from individual studies using the following dosages: AMP/r 600mg/100mg BID; ATV/r 300mg/100mg QD; DRV/r 600mg/100mg BID; IDV/r 800mg/200mg BID; LPV/r 400mg/100mg BID; SQV/r 1000mg/100mg BID; and TPV/r 500mg/200mg BID.

Assessment of drug susceptibility is based upon detected mutations and interpreted using an advanced proprietary algorithm (version 14)

Patient-Specific Results

Drugs	ABC	ddI	FTC	3TC	d4T	ZDV	TFV	DLV	EFV	ETR	NVP	RPV	ATV	DRV	AMP	IDV	LPV	NFV	RTV	SQV	TPV
IC50 (µM)	6.6	11.56	>100	>300	1.4	0.349	1.274	0.118	0.1157	0.001315	>20	0.001275	0.00999	0.001211	0.0567	0.0408	0.0121	0.2611	0.163	0.0197	0.3945
Fold Change	3.98	1.99	>MAX	>MAX	1.51	7.91	1.16	3.91	30	0.56	>MAX	1.29	4.96	1.34	4.00	5.81	1.69	17	4.30	3.88	2.87

For more information on interpreting this report, please visit www.MonogramHIV.com or call Customer Service at 800-777-0177 between the hours of 6:30am to 5:00pm PT Monday through Friday.