PhenoSense GT® PLUS INTEGRASE

Monogram BIOSCIENCES
LabCorp Specialty Testing Group

Samuel H. Pepkowitz, MD, Medical Director
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South San Francisco, CA 94080 - Tel: (800) 777-0177

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 Class	Generic Name	Brand Name	Net Assessment	Cutoffs (Lower-Upper)	Fold Change	Pheno Type	Geno Type	Comments
NRTI	**Abacavir**	Ziagen	Sensitive	*(4.5 - 6.5)*	3.98	Y	N	16
	Didanosine	Videx	Partially Sensitive	*(1.3 - 2.2)*	1.99	P	N	
	Emtricitabine	Emtriva	Resistant	*(3.5)*	>MAX	N	N	
	Lamivudine	Epivir	Resistant	*(3.5)*	>MAX	N	N	
	Stavudine	Zerit	Sensitive	*(1.7)*	1.51	Y	N	3
	Zidovudine	Retrovir	Resistant	*(1.9)*	7.91	N	N	3
	Tenofovir	Viread	Sensitive	*(1.4 - 4)*	1.16	Y	P	3
	NRTI Mutations		**M41L, M184V, T215Y**					
NNRTI	**Delavirdine**	Rescriptor	Partially Sensitive	*(6.2)*	3.91	Y	P	1
	Efavirenz	Sustiva	Resistant	*(3)*	30	N	N	
	Etravirine	Intelence	Partially Sensitive	*(2.9 - 10)*	0.56	Y	P	1
	Nevirapine	Viramune	Resistant	*(4.5)*	>MAX	N	N	
	Rilpivirine	Rilpivirine	Resistant	*(2.5)*	1.29	Y	N	1
	NNRTI Mutations		**Y188Y/F/L, H221H/Y**					
INI	**Dolutegravir**	Tivicay	Sensitive	*(4 - 13)*	3.41	Y	P	16
	Elvitegravir	Elvitegravir	Resistant	*(3.5)*	>MAX	N	N	
	Raltegravir	Isentress	Resistant	*(2.2)*	>MAX	N	N	
	INI Mutations		**G140S, Q148H**					

DRUG | PHENOSENSE® SUSCEPTIBILITY | Evidence of Susceptibility

Drug Susceptibility: Increasing ◄ 1 — 10 — 100 ► Decreasing

PI

Results for Protease Inhibitors are shown on page 2 of this report

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:

	DRUG			PHENOSENSE® SUSCEPTIBILITY				Evidence of Susceptibility		
Drug Class	Generic Name	Brand Name	Net Assessment	Cutoffs (Lower-Upper)	Fold Change	Increasing ← Drug Susceptibility → Decreasing (1, 10, 100)		Pheno Type	Geno Type	Comments
PI	**Atazanavir**	Reyataz	**Resistant**	*(2.2)*	**4.96**			**N**	**N**	
PI	**Atazanavir**	Reyataz / r‡	**Sensitive**	*(5.2)*	**4.96**			**Y**	**P**	16
PI	**Darunavir**	Prezista / r‡	**Sensitive**	*(10 - 90)*	**1.34**			**Y**	**Y**	
PI	**Fosamprenavir**	Lexiva / r‡	**Sensitive**	*(4 - 11)*	**4.00**			**Y**	**Y**	
PI	**Indinavir**	Crixivan / r‡	**Sensitive**	*(10)*	**5.81**			**Y**	**Y**	
PI	**Lopinavir**	Kaletra‡	**Sensitive**	*(9 - 55)*	**1.69**			**Y**	**Y**	
PI	**Nelfinavir**	Viracept	**Resistant**	*(3.6)*	**17**			**N**	**N**	
PI	**Ritonavir**	Norvir	**Resistant**	*(2.5)*	**4.30**			**N**	**N**	
PI	**Saquinavir**	Invirase / r‡	**Partially Sensitive**	*(2.3 - 12)*	**3.88**			**P**	**P**	
PI	**Tipranavir**	Aptivus / r‡	**Partially Sensitive**	*(2 - 8)*	**2.87**			**P**	**P**	
	PI Mutations		**L10V, I13V, K20T, E35G, M36I, I62V, L63T, T74S, L90M**							

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.

Combination Phenotype/Genotype Net Assessment

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

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

PhenoSense GT plus Integrase is an assay that combines the proprietary technology of PhenoSense with a genotypic assessment of resistance and expert interpretation for HIV-1 reverse transcriptase, protease and integrase inhibitors in a single report. PhenoSense is a proprietary, recombinant virus, single replication cycle phenotypic assay. The genotypic DNA sequence assay is performed using primer extension and chain termination to analyze the protease (amino acids 1-99), reverse transcriptase (amino acids 1-400) and integrase (amino acids 1-288) coding regions in HIV-1 DNA sequences amplified from a patient blood sample to evaluate mutational changes associated with drug resistance. HIV-1 subtype is determined using the protease and reverse transcriptase sequence information. This assay meets the standards for performance characteristics and all other quality control and assurance requirements established by the Clinical Laboratory Improvement Amendments. This test 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. The 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.

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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

IN: S17N, V31I, I84V, T112T/I, T124N, Q137Q/H, G140S, Q148H, M154I, V165I, V201I, T218S, Y227F, V234L, S255N, D256E

Patient-Specific Results

Drugs	ABC	ddI	FTC	3TC	d4T	ZDV	TFV	DLV	EFV	ETR	NVP	RPV
IC50(µM)	6.6	11.56	>100	>300	1.4	0.349	1.274	0.118	0.1157	0.001315	>20	0.001275
Drugs	**DTG**	**EVG**	**RAL**	**ATV**	**DRV**	**AMP**	**IDV**	**LPV**	**NFV**	**RTV**	**SQV**	**TPV**
IC50(µM)	0.011106	>0.7	>2	0.00999	0.001211	0.0567	0.0408	0.0121	0.2611	0.163	0.0197	0.3945

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 12)