



www.vicolab.com

Virco BVBA  
Generaal de Wittelaan L11 B4  
B-2800 Mechelen, Belgium

Inquiries to:  
Lab21, Cambridge, UK  
Tel: +44(0) 1223 395450  
Email: info@lab21.com  
Web: www.lab21.com



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# vircoTYPE HIV-1

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Resistance Analysis of HIV-1 Protease and Reverse Transcriptase

Patient/Sample Details				Physician Details	
CONFIDENTIAL	Patient Initials	ABC	Lab21 ID	EXAMPLE1	CLINIC
			Sample Date	20-May-2010	DEPT
	Patient ID	Pat-123-456	Received by Lab21	21-May-2010	ADDRESS1
	Customer Number	CN-101	Report Date	25-May-2010	CITY STATE ZIP
	Date of birth	01-Aug-1966	Virco ID	ZAF002001	COUNTRY
					Physician: Dr. FIRST LAST

## SUMMARY REPORT

DRUGS		FOLD CHANGE <sup>1</sup>	CUT-OFF <sup>2</sup>		RESISTANCE ANALYSIS <sup>3</sup>	CLINICAL NOTES (see p2 for details)	
<b>NRTI / NtRTI mutations<sup>4</sup>: 41L, 44D, 67N, 74V, 181C, 184V, 210W, 215Y, 219R, 335D</b>							
NRTI/NtRTI	Retrovir®	Zidovudine	8.3	1.5	11.4	REDUCED RESPONSE	
	Epivir®	Lamivudine	44.8	2.1	4.6	MINIMAL RESPONSE	
	Videx®	Didanosine	3.1	0.9	2.6	MINIMAL RESPONSE	
	Zerit®	Stavudine	1.7	1.0	2.3	REDUCED RESPONSE	
	Ziagen®	Abacavir	6.5	0.9	3.5	MINIMAL RESPONSE	
	Emtriva®	Emtricitabine	34.8	3.1		RESISTANT	
	Viread®	Tenofovir DF	1.5	1.0	2.3	REDUCED RESPONSE	

### NNRTI mutations<sup>4</sup>: 98G, 101H, 181C, 190A

NNRTI	Viramune®	Nevirapine	94.2	6.0		RESISTANT	
	Sustiva®, Stocrin®	Efavirenz	185.8	3.3		RESISTANT	
	Intelence™	Etravirine	2.6	3.2	27.6	SUSCEPTIBLE	Note 1,2

### PI mutations<sup>4</sup>: 10F, 15V, 20R, 36I, 43T, 46I, 54L, 63P, 69K, 71V, 74P, 82A, 84V, 90M, 93L

PI	Crixivan®; boosted	Indinavir/r	20.0	2.3	27.2	REDUCED RESPONSE	
	Viracept®	Nelfinavir	53.8	2.2	9.4	MINIMAL RESPONSE	
	Invirase®; boosted	Saquinavir/r	36.0	3.1	22.6	MINIMAL RESPONSE	
	Lexiva®, Telzir®; boosted	Fosamprenavir/r	36.8	1.5	19.5	MINIMAL RESPONSE	
	Kaletra®	Lopinavir/r	36.1	6.1	51.2	REDUCED RESPONSE	
	Reyataz®; boosted	Atazanavir/r	60.0	2.5	32.5	MINIMAL RESPONSE	
	Aptivus®; boosted	Tipranavir/r	1.5	1.5	7.0	MAXIMAL RESPONSE	Note 1
	Prezista™; boosted	Darunavir/r	13.9	10.0	106.9	REDUCED RESPONSE	

1. Predicted Fold Change in 50% Inhibitory Concentration (IC<sub>50</sub>), relative to susceptible reference virus. 2. Cut-off values for maximal and minimal clinical response (Clinical Cut-Off) or for normal susceptibility range *in vitro* (Biological Cut-Off). Biological Cut-Offs are printed in italic. See page 3 for definitions. 3. Resistance Analysis based on the magnitude of the Fold Change relative to the Clinical or the Biological Cut-Offs. See page 3 for definitions. 4. Mutations printed on page 1 are those reported on public lists (ANRS, Stanford, IAS-USA) or by drug development sponsors. A complete list of all differences from the reference wild type is given on page 2.

IMPORTANT: the additional clinical notes on page 2 provide important information about the specific genotype analysed and should be considered in combination with information on this Summary Page.

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ANALYZED SEQUENCE REGION		CLADE	PATIENT ID	VIRCO ID
PR 1 - 99	RT 1 - 400	C	Pat-123-456	ZAF002001

DRUGS	0.3	1	10	100	200	FC	(95% confidence limits)	CCO 1	CCO 2	BCO
Zidovudine AZT						8.3	(7.2-9.6)	1.5	11.4	
Lamivudine 3TC						44.8	(42.8-46.9)	1.2	4.6	2.1
Didanosine ddl						3.1	(2.8-3.3)	0.9	2.6	
Stavudine d4T						1.7	(1.5-1.9)	1.0	2.3	
Abacavir ABC						6.5	(6.2-6.9)	0.9	3.5	
Emtricitabine FTC						34.8	(31.4-38.6)			3.1
Tenofovir DF TDF						1.5	(1.4-1.7)	1.0	2.3	
Nevirapine NVP						94.2	(79.8-111.1)			6.0
Efavirenz EFV						185.8	(136.0-253.8)			3.3
Etravirine ETR						2.6	(2.1-3.1)	1.6	27.6	3.2
Indinavir/r IDV/r						20.0	(17.1-23.3)	2.3	27.2	
Nelfinavir NFV						53.8	(47.8-60.5)	1.2	9.4	2.2
Saquinavir/r SQV/r						36.0	(31.8-40.7)	3.1	22.6	
Fosamprenavir/r FPV/r						36.8	(33.2-40.8)	1.5	19.5	
Lopinavir/r LPV/r						36.1	(31.8-41.1)	6.1	51.2	
Atazanavir/r ATV/r						60.0	(51.2-70.2)	2.5	32.5	
Tipranavir/r TPV/r						1.5	(1.4-1.7)	1.5	7.0	
Darunavir/r DRV/r						13.9	(11.8-16.4)	10.0	106.9	

## All Mutations Detected (HXB2 Reference Sequence)

PR: 3I, 10F, 15V, 19I, 20R, 36I, 37N, 43T, 46I, 54L, 63P, 69K, 71V, 74P, 82A, 84V, 90M, 93L

RT: 35L, 39E, 41L, 44D, 67N, 74V, 98G, 101H, 111I, 122P, 158S, 173T, 174K, 177E, 181C, 184V, 190A, 200A, 203K, 207E, 208Y, 210W, 211K, 214F, 215Y, 218E, 219R, 223Q, 245Q, 277K, 291D, 292I, 293V, 334D, 335D, 356K, 357R, 359T, 376A, 377L, 390R, 400A

## Additional Clinical Notes

### Note 1

The CCOs for these drugs are based on treatment responses in select populations of treatment-experienced patients participating in Phase II or III clinical trials of these new agents. The relevance of these CCOs for patients different from these study participants has not been evaluated. For more information about the datasets used to calculate vircoTYPE HIV-1 clinical cut-offs, please refer to [www.vircotype-references.com](http://www.vircotype-references.com)

### Note 2

The resistance interpretation for this sample has been made using the BCO of 3.2 instead of the lower CCO of 1.6. In the Virco genotypic database, substantial numbers of viruses with no evidence of acquired drug resistance have an ETR FC between 1.6 and 3.2. Therefore, this report classifies all isolates with ETR FC less than or equal to the BCO of 3.2 as Susceptible.



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DEFINITIONS

1. Calculated FC values

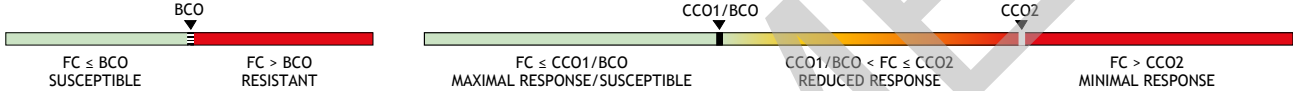
Phenotypic FC values are predicted from the viral genotype using the virtualPhenotype-LM bioinformatics tool [Vermeiren et al., J. Virol. Meth. 145 (2007) 47]. When mixtures are detected in the viral genotype, the prediction is based on the variant at each position with the highest level of resistance, thus providing a conservative prediction of FC or potential resistance. See www.vircotype-references.com for additional details.

2. Cut-Off values

Biological cut-off values (BCO) are an indication of the normal range of susceptibility of wild type HIV-1 strains to each drug in an in vitro laboratory assay; Clinical cut-off values (CCO) are based on observations of virologic response (change in Viral Load) in treated patients and give an indication of how that response is affected by viral resistance. The lower clinical cut-off (CCO1) is the baseline Fold Change in IC50 below which the virologic response to a drug is expected to be similar to that of a wild type virus, but above which the response to that drug begins to decline due to viral resistance. The upper clinical cut-off (CCO2) is the baseline Fold Change in IC50 above which most virologic response to the drug is expected to be lost due to resistance. See www.vircotype-references.com for more information and 90% confidence intervals. The colored bar on page 2 represents the drug-specific dynamic range of resistance for each drug, ranging from the predicted FC for wild type isolates to the 97.5th percentile of FC predictions.

3. Resistance Analysis

The analysis of HIV-1 susceptibility on the first page of this report is based on the magnitude of the Fold Change in IC50 (FC) relative to cut-off values.



4. Additional Clinical Notes

Additional Clinical Notes provide clinical information that might be relevant for the sample virus. These notes are established by an international panel of virologists and clinicians and updated regularly.

5. Method description

The genotyping assay: HIV-1 genomic information corresponding to part of the protease and reverse transcriptase genes was determined by standard viral isolation, PCR amplification and DNA sequencing methodologies. The analyzed sequence region is shown on page 2.

The virco@TYPE HIV-1 analysis: The sequence result was aligned and mutations were identified. Calculated FC values were determined using a proprietary analysis technology optimized for sequences covering codons 1-99 for Protease and codons 1-400 of Reverse Transcriptase. Sequences which at a minimum cover codons 10 - 95 in Protease and 41- 238 in RT are accepted for analysis by this method. Resistance analysis results were obtained using FC and cut-off values. Clade assignments are based on similarity of the analyzed sequence to the subtype references of the Los Alamos National laboratory HIV database and apply to the reported sequence region.

DISCLAIMERS

- This is a complete report. The result relates only to the item tested.
This report shall not be reproduced, except in full, without the written approval of the testing laboratory.
A patient's response to therapy depends on multiple factors, including the percentage of a patient's viral population that is drug-resistant, patient compliance, lack of access to adequate care, drug pharmacokinetics and drug interactions. Therefore, this test should be used only in conjunction with clinical presentation and other laboratory markers (e.g. symptoms, treatment history, clinical impressions, results from other tests, etc.) when making therapy decisions. Consultation with an expert in HIV drug resistance is encouraged to facilitate clinical application of the test results.
This test may be unsuccessful if the plasma HIV RNA viral load is < 1000 copies of virus per ml of plasma, measured with the Amplicor® HIV Monitor test (Roche Diagnostics).
For NY State only: "This test result is confidential HIV information and may not be redisclosed except as outlined by NY State Law (art. 27F)".
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The genotyping assay was developed and its performance characteristics determined by the testing laboratory. The sequence results were generated by the testing laboratory. Virco cannot be held responsible for the quality, integrity and the correctness of the sequence results, or for the correctness of patient demographic data added to this report. The virco@TYPE HIV-1 analysis method was developed and its performance characteristics determined by Virco.
Submitted sequences shorter than the optimal length (see 5. Method description) may result in less accurate virco@TYPE HIV-1 results.

SEQUENCE SUBMITTED FOR INTERPRETATION

CCTCAAATCACTCTTTGGCCAGCAGCCCTTTGTCAATAAAAAGTAGGGGACAGATAAGGGAGGCTCTCTTAGACACAGGAGCAGATGATACAGTATTAGAAGAAAATAAATTTGCTTGGAAAGTGGACACCA
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TCAGATTACCTATCCAGAAAGAAACATGGGAAGCA

Testing Laboratory
Molecular Biology and Genotyping :
Lab21, 184 Cambridge Science Park, Cambridge, CB4 0GA, UK
Tel: +44 (0)1223 395450, Fax: +44 (0)1223 395451, Email: info@lab21.com