Micropathology Ltd

The Venture Centre, University of Warwick Science Park, Sir William Lyons Road, Coventry, United Kingdom, CV4 7EZ
www.micropathology.com ✉ info@micropathology.com ☎ +44(0)2476 323222

HIV-1 Protease and Reverse Transcriptase Drug Resistance Report

Using next generation sequencing (NGS) to detect mutations down to 5% relative frequency

Micropathology Lab Number: 1234567 **Date:** 17/04/2025

Your Patient/Lab Number: M12345

The following report summarizes apparent antiretroviral drug resistance. It is based upon an analysis* of protease and reverse transcriptase gene sequences of the HIV-1 virus amplified from the supplied specimen (see laboratory numbers above). Additional information detailing the HIV-1 subtype and a quality assessment of the sequence data is also included. The report utilises the following abbreviations: PR = Protease, PI = Protease Inhibitor, RT = Reverse Transcriptase, RTI = Reverse Transcriptase Inhibitor, TAMs = Thymidine Analogue-associated Mutations, SDRMs = Surveillance Drug Resistance Mutations.

Please note, we sequenced and analysed the PR/RT amplicon using next generation sequencing (NGS) methods (awaiting UKAS-accreditation). A nucleotide variant is reported if it occurs in a proportion of the reads at or above the minimum nucleotide frequency threshold which was set at **5%**. The relative frequencies of drug resistance mutations are denoted only where a heterogeneous population is present at a particular site.

* Analysis performed using the Stanford Genotypic Resistance Interpretation Algorithm Version 9.8.

Result: Drug resistance associated mutations observed

SUMMARY DATA:

Sequence includes PR:	codons 10 - 99
Sequence includes RT:	codons 1 - 348
Subtype:	C (5.71%)
PR SDRMs:	None
RT SDRMs:	**K65KR (12%), L100I, K103N, M184MV (25%), K219E**

SEQUENCE QUALITY ASSESSMENT:

PASSED

DRUG RESISTANCE INTERPRETATION:

PR Mutations

PI Major Mutations:	None
PI Accessory Mutations:	None
PR Other Mutations:	T12S, I15V, L19T, K20R, E35D, M36I, N37D, K45R, R57K, L63T, H69K, V82I, L89M, I93L

Protease Inhibitors

atazanavir/r (ATV/r)	Susceptible
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Susceptible
indinavir/r (IDV/r)	Susceptible
lopinavir/r (LPV/r)	Susceptible
nelfinavir (NFV)	Susceptible
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Susceptible

PR comments

Other

- K20R is a highly polymorphic PI-selected accessory mutation that increases replication fitness in viruses with PI-resistance mutations.
- V82I is a highly polymorphic mutation that is not selected by PIs. It is the consensus amino acid in subtype G viruses.

RT Mutations

NRTI Mutations:	**K65KR (K65R: 12%), S68G, M184MV (M184V: 25%), K219E**
NNRTI Mutations:	**L100I, K103N**
RT Other Mutations:	K20R, V35R, T39E, S48T, A98S, K122E, D123N, I135T, I142T, S162A, Q174K, D177E, V179I, G196E, T200A, E203D, Q207A, R211K, D237E, V245Q, E248D, A272P, T286A, V292I, I293V, S322T, I329L, Q334D

Nucleoside Reverse Transcriptase Inhibitors

abacavir (ABC)	**High-Level Resistance**
zidovudine (AZT)	Susceptible
stavudine (D4T)	**High-Level Resistance**
didanosine (DDI)	**High-Level Resistance**
emtricitabine (FTC)	**High-Level Resistance**
lamivudine (3TC)	**High-Level Resistance**
tenofovir (TDF)	**Intermediate Resistance**

Non-nucleoside Reverse Transcriptase Inhibitors

doravirine (DOR)	**Intermediate Resistance**
dapivirine (DPV)	**High-Level Resistance**
efavirenz (EFV)	**High-Level Resistance**
etravirine (ETR)	**Intermediate Resistance**
nevirapine (NVP)	**High-Level Resistance**
rilpivirine (RPV)	**High-Level Resistance**

RT comments

NRTI

- **K65R** confers intermediate reductions in susceptibility to TDF, ABC, and 3TC/FTC. Other than M184VI, it is the most common DRM emerging in patients receiving TDF/XTC. K65R increases AZT susceptibility. In NRTI-experienced, INSTI-naive patients with K65R, TDF/3TC/DTG is usually highly effective and more effective than AZT/3TC/DTG. However, in patients receiving TDF/3TC/DTG, there is a risk of emergent DTG resistance that does not arise in NRTI-naive patients receiving TDF/3TC/DTG.
- **S68G** is a polymorphic mutation that is often selected in combination with K65R. It partially restores the replication defect associated with K65R.
- **M184V/I** cause high-level in vitro resistance to 3TC and FTC and low/intermediate resistance to ABC (3-fold reduced susceptibility). M184V/I are not contraindications to continued treatment with 3TC or FTC because they increase susceptibility to AZT and TDF and are associated with clinically significant reductions in HIV-1 replication.
- **K219E/Q/N/R** are accessory TAMS that usually occur in combination with multiple other TAMs.

NNRTI

- **L100I** is a non-polymorphic mutation that usually occurs in combination with K103N. In this setting it confers high-level resistance to NVP, EFV, and RPV and intermediate resistance to ETR and DOR.
- **K103N** is a non-polymorphic mutation that confers high-level reductions in NVP and EFV susceptibility. It is the most commonly transmitted DRM.

Other

- **V179I** is a polymorphic mutation that is frequently selected in persons receiving ETR and RPV. However, it has little, if any, direct effect on NNRTI susceptibility.