



Second-Line ART After Treatment Failure or for Regimen Simplification

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Table 1: Types of HIV Resistance Tests [a]		
Test	Description	Use
Genotype	<ul style="list-style-type: none"> Assesses mutations in the HIV RNA genes that encode enzymes targeted by ARVs: reverse transcriptase, protease, integrase Algorithms interpret the effect of mutations on ARV efficacy 	<ul style="list-style-type: none"> At diagnosis, when a patient has incomplete virologic response to ART, or when viral rebound occurs Has utility if plasma HIV-1 RNA level (viral load) is ≥ 500 to 1,000 copies/mL May not detect all RAMs
Phenotype	<ul style="list-style-type: none"> Assesses the effect of HIV genes on the ARV concentration required to inhibit viral growth compared with wild-type (nonmutant) virus Estimates a fold change 	<ul style="list-style-type: none"> Historically used to help assess the effect of the interplay of multiple RAMs on viral growth Supplanted by more comprehensive genotypic interpretation algorithms
Proviral DNA genotype (archived genotype)	<ul style="list-style-type: none"> Assesses genetic mutations in HIV proviral DNA genes that encode enzymes targeted by ARVs: reverse transcriptase, protease, and integrase Algorithms interpret the effect of mutations on ARV efficacy 	<ul style="list-style-type: none"> When planning ART simplification or other changes, may have a role in identifying RAMs when standard genotype testing may not yield results, i.e., in patients who have prior treatment experience, have stopped taking ARVs for >4 weeks, or have an HIV viral load <500 to 1,000 copies/mL or below the limit of quantification May not detect all RAMs or report RAMs from defective non-replication-competent proviral DNA [Li, et al. 2021]
Tropism test	Assesses the effect of HIV RNA (or proviral DNA) gp120 on the coreceptor(s) used for viral attachment: CCR5, CXCR4, or mixed/dual	<ul style="list-style-type: none"> Treatment-experienced patients for whom a coreceptor antagonist is being imminently considered RNA tropism test can be used with viral loads $\geq 1,000$ copies/mL; proviral DNA test can be used for viral loads <1,000 copies/mL
<p>Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral medication; gp120, envelope glycoprotein 120; RAM, resistance-associated mutation.</p> <p>Note:</p> <p>a. All resistance assays are affected by limitations of detection; minor variants may not be present at high enough concentrations to be amplified by the assay.</p>		

Table 3: Genotypic Resistance Testing Based on Viral Load	
HIV RNA (Viral Load)	Indicated Genotypic Resistance Test
0 to 500 copies/mL	HIV proviral DNA genotype (RT, PR, INT) or phenotype (tropism)
500 to 1,000 copies/mL	HIV RNA genotype (RT, PR, INT) or phenotype (tropism) at assay amplification threshold; may use HIV proviral DNA test if nonamplifiable
$\geq 1,000$ copies/mL	HIV RNA genotype if currently or recently (within 4 weeks) on ART; DNA proviral genotype may be considered for patients who are currently not taking ART but have in the past
<p>Abbreviations: ART, antiretroviral therapy; INT, integrase; PR, protease; RT, reverse transcriptase.</p>	

Reference

Li Y, Etemad B, Dele-Oni R, et al. Drug resistance mutations in HIV provirus are associated with defective proviral genomes with hypermutation. *AIDS* 2021;35(7):1015-1020. [PMID: 33635848] <https://pubmed.ncbi.nlm.nih.gov/33635848>