Appendix 2. Summary of DHHS Testing Recommendations for Selecting Antiretroviral Treatment

Clinical Setting

General Recommendations

- ART-naïve patients
  - ART, antiretroviral treatment; DHHS, Department of Health and Human Services; INSTI, integrase strand transfer inhibitor.

- Pharmacogenetic screening for the HLA-B*5701 allele is recommended for abacavir-naïve patients before initiation of an abacavir-containing regimen, as this allele predicts hypersensitivity to abacavir.
- Resistance testing may still provide useful information more than 4 weeks after discontinuation of ART, but previously selected resistance mutations can be missed.

Specific Recommendations

- Patients with integrase failure
  - Resistance testing should be performed on samples obtained while the patient is on an active antiretroviral regimen.

- Patients failing NRTI-based regimens
  - INSTI genotype testing is recommended if transmitted INSTI resistance is a concern.

- Patients failing NNRTI-based regimens
  - Drug resistance testing is recommended on a patient’s current antiretroviral regimen.

- Patients failing PI-containing regimens
  - INSTI resistance testing should be performed on samples obtained while the patient is on a PI-containing antiretroviral regimen.

- Patients being considered for an INSTI-containing regimen
  - INSTI resistance testing should be performed on samples obtained while the patient is on a regimen that does not contain any INSTI.

References


Figure 1

Select antiretroviral regimen containing s2 active drugs from s2 classes

Resistance testing

HIV drug resistance can be evaluated with genotyping or phenotyping. For the approach, resistance testing should be performed on samples obtained at the patient’s request or when the patient is receiving the failing regimen or soon after discontinuation; otherwise, resistant variants may not be detected but may re-emerge if the drug is reinstated. Therapy decisions should also take into account the results of previous resistance testing.
Genotypic Testing

Genotypic HIV resistance tests identify drug resistance-associated mutations in patient specimens from infected individuals. Relative to phenotypic testing, genotypic testing is considered to be more accurate and reliable for determining the susceptibility of a virus to antiretroviral therapies and is typically more applicable in the following situations:

- Initially infected with multidrug-resistant virus
- Patient developing virologic failure
- Complex mutation patterns and benefit from addition of phenotypic analysis
- Expert advice is recommended when assessing cross-resistance
- HIV-1 phenotype if >2 N(t)RTI(s)/NNRTI/PI

Phenotypic Testing

Phenotypic testing involves allowing the HIV to replicate in the presence of potential antiretroviral drugs, without regard to specific mutations present in the virus population. A useful recombinant HIV-1 virus is created consisting of a reference virus with selected mutations derived from the patient’s virus. This assay determines whether the virus replicates in the presence of a drug in the event of drug resistance mutations. The fold change is evaluated against a clinical cutoff value to determine whether the virus remains susceptible to each drug. Because phenotypic testing reflects the drug effect of HIV mutations, it may be particularly useful in high mutation settings.

Table 1 summarizes some of the key differentiating features of genotypic and phenotypic testing.

What the Guidelines Say

Genotypic assays are currently recommended at an earlier stage of the treatment management plan than phenotype for the following reasons:

- Greater sensitivity
- Direct in vitro measurement
- Lower cost
- Higher specificity
- Qualitative assessment
- Greater sensitivity than cross-resistance tests
- More time-saving detection

OTHER TESTS USED IN SELECTING HIV ARVs

HIV-1 Coreceptor Tropism Assay

HIV-1 coreceptor tropism testing determines eligibility for treatment with CCR5 antagonists. HIV-1 utilizes the CD4 cell surface receptor and either the CCR5 or CXCR4 co-receptor for entry into target cells. CCR5 antagonists are reserved for R5-tropic viruses that exclusively utilize the CCR5 coreceptor. HIV-1 utilizes the CD4 cell surface receptor and either the CCR5 or CXCR4 co-receptor for entry into target cells. CCR5 antagonists are reserved for R5-tropic viruses that exclusively utilize the CCR5 coreceptor.

Table 2. Use of HIV Drug Resistance Testing at Different Stages of Disease Management

<table>
<thead>
<tr>
<th>Stage of HIV Disease</th>
<th>Indication</th>
<th>Test Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute HIV infection</td>
<td>Antiretroviral(s)</td>
<td>Genotypic</td>
</tr>
<tr>
<td>Primary HIV infection</td>
<td>Antiretroviral(s)</td>
<td>Genotypic</td>
</tr>
<tr>
<td>Late-stage HIV infection</td>
<td>Antiretroviral(s)</td>
<td>Genotypic</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>Antiretroviral(s)</td>
<td>Genotypic</td>
</tr>
</tbody>
</table>

Appendix 1. Laboratory Tests Used in Guiding Selection of Antiretroviral Drugs

- For additional testing options, consult the Quest Diagnostics online Test Center (QuestDiagnostics.com/TestCenter).
- The Quest Diagnostics test is also comparable to other commercially available testing options for detection of minority X4 virus in D/M viral populations.
- The Quest Diagnostics test is also comparable to other commercially available testing options for detection of minority X4 virus in D/M viral populations.