Table 23. Summary of Guidelines for Changing an Antiretroviral Regimen for Suspected Treatment Regimen Failure

**Patient Assessment (AIII)**
- Review antiretroviral treatment history.
- Assess for evidence of clinical progression (e.g., physical exam, laboratory and/or radiologic tests).
- Assess adherence, tolerability, and pharmacokinetic issues.
- Distinguish between limited, intermediate, and extensive prior therapy and drug resistance.
- Perform resistance testing while patient is taking therapy (or within 4 weeks after regimen discontinuation).
- Identify active drugs and drug classes to use in designing the new regimen.

**Patient Management: Specific Clinical Scenarios**

- **Limited or intermediate prior treatment with low (but not suppressed) HIV RNA level (e.g., up to 5000 copies/mL):** The goal of treatment is to re-suppress HIV RNA to below the level of assay detection. Consider intensifying with one drug (e.g., tenofovir) (BII) or pharmacokinetic enhancement (use of ritonavir boosting of a protease inhibitor) (BII), perform resistance testing if possible, or most aggressively, change two or more drugs in the regimen (CIII). If continuing the same treatment regimen, HIV RNA levels should be followed closely because ongoing viral replication will lead to accumulation of additional resistance mutations.

- **Limited or intermediate prior treatment with resistance to one drug:** Consider changing the one drug (CIII), pharmacokinetic enhancement (few data available) (BII), or, most aggressively, change two or more drugs in the regimen (BII).

- **Limited or intermediate prior treatment with resistance to more than one drug:** The goal of treatment is to suppress viremia to prevent further selection of resistance mutations. Consider optimizing the regimen by changing classes (e.g., PI-based to NNRTI-based and vice versa) and/or adding new active drugs (AIII) (See Table 25: Treatment options following virologic failure on initial recommended therapy regimens.)

- **Prior treatment with no resistance identified:** Consider the timing of the drug resistance test (e.g., was the patient off antiretroviral medications?) and/or nonadherence. Consider resuming the same regimen or starting a new regimen and then repeating genotypic testing early (e.g., 2–4 weeks) to determine if a resistant viral strain emerges on treatment (CIII).

- **Extensive prior treatment and drug resistance:** In patients with active antiretroviral agents available (e.g., an active ritonavir-boosted PI and enfuvirtide), the goal of therapy is suppression of viremia. In patients without active antiretroviral agent available and with ongoing viremia, the goal of therapy is preservation of immune responses and delay of clinical progression. It is reasonable to continue the same antiretroviral regimen if there are few or no treatment options (CIII). In general, avoid adding a single active drug because of the risk for the rapid development of resistance to that drug. In advanced HIV disease with a high likelihood of clinical progression (e.g., CD4 cell count <100 cells/mm³), adding a single drug may reduce the risk of immediate clinical progression (CIII). In this complicated scenario, expert advice should be sought (See Table 24: Novel strategies to consider for treatment-experienced patients with few available active treatment options.)

- **Immunologic failure (or blunted CD4 response) with virologic suppression:** Immunologic failure (or blunted CD4 cell response) may not warrant a change in therapy in the setting of suppressed viremia. Assess for other causes of immunosuppression (e.g., HIV-2, HTLV-1, drug toxicity). The combination of didanosine and tenofovir has been associated with CD4 cell declines or blunted CD4 cell responses. In the setting of immunologic failure (or blunted CD4 response), it would be reasonable to change one of these drugs (BIII). Intensifying with additional antiretroviral drugs or the use of immune-based therapies (e.g., interleukin-2) to improve immunologic responses remain unproven strategies and generally should not be offered (DII).