Is It Time to Perform HIV Drug Resistance Testing Prior to Initiate Antiretroviral Therapy Among HIV-infected Patients in Thailand?

Somnuek Sungkanuparph, M.D.

It is well known that HIV can mutate, reducing its susceptibility to antiretroviral agents, and that these resistant viruses can be transmitted from person-to-person through contact with blood or blood products, sexual intercourse or from mother-to-child.1,2,3 There is strong evidence that HIV-infected patients with primary drug resistance are at a higher risk of virological failure4,5 or longer time to virological suppression under the first-line antiretroviral therapy (ART).5-8 The longer time to achieve complete virological suppression may permit viral replication to select for additional drug-resistant variants,9 which could lead to treatment failure. The emergence of primary drug resistance is a major public health problem; it has been associated with increased morbidity, mortality, and medical costs.5,10

The prevalence of primary drug resistance varies as ART is widely used in a given population.3 Increased rates of secondary drug resistance in the HIV-infected population due to suboptimal therapy tend to be followed by increases in the prevalence of primary drug resistance.11 The prevalence of primary resistance in developed countries ranges from 8% to 19%.12-16 By drug class, resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) has markedly increased in the last decade, due to the widespread use of NNRTIs coupled with their low genetic barrier. Protease inhibitor (PIs) resistance is generally less frequent.3,17

To date, rates of primary HIV drug resistance have been increasing after the high frequency of secondary drug resistance in several resource-limited settings. The reported prevalence of primary drug resistance in various countries in sub-Saharan Africa ranged from 2.1% to 14.8% of patients initiating first-line ART.19-24 Among treatment-naive patients in western India, drug resistance was documented in 10% of patients.25 In Brazil and Argentina, rates of transmitted drug resistance range from 3.1% to 22.2%.26-31 Therapeutics, Research, Education and AIDS Training in Asia (TREAT Asia), a network of clinics, hospitals, and research institutions in Asia, had initiated the TREAT Asia Studies to Evaluate Resistance-Monitoring Study (TASER-M) and recently published the results showing that primary HIV drug resistance is emerging after rapid scaling-up of antiretroviral therapy use in Asia.32

In Thailand, National AIDS Program (NAP) has provided free access to ART for scaling up HIV treatment since 2002.33 The previous published data had shown that only 2% of patients with recent infection had primary HIV drug resistance.34 However, when patients were categorized by year of blood test, the rate increased from 0% in 2003 to 5.2% in 2006. Importantly, all seven patients with primary drug resistance had sexual partner with low adherence (<75%) with NNRTI-based regimen. This data strongly suggested that HIV drug resistance was transmitted.
among couples. Recently, a study to determine the prevalence of drug resistance among antiretroviral-naive patients in Bangkok was conducted.\(^{35,36}\) In this study, the surveillance drug resistance mutations (SDRMs) recommended for surveillance of transmitted HIV-1 drug resistance by World Health Organization (WHO) in 2009 was used.\(^{37}\) The results of the study revealed that 5.3% of all patients had primary drug resistance. When patients were categorized into three groups according to the risk of HIV infection: heterosexual, homosexual and intravenous drug user, the prevalence of primary drug resistance was 4.5%, 3.4% and 20%, respectively.\(^{35}\) This alarms us the high rate of primary HIV drug resistance in intravenous drug users in Bangkok.

When treatment of patients who have failed antiretroviral therapy is guided by expert interpretation of genotypic resistance, significantly improved virological outcome is achieved.\(^{38-40}\) In addition, a cohort study has recently demonstrated that use of resistance testing to guide the selection of ART was independently associated with improved survival among treatment-experienced patients.\(^{41}\) Although these results cannot easily be extrapolated to the case of primary drug resistance, it is likely to be similar due to the impact of NNRTI resistance on the first-line ART and limited options of antiretroviral regimen in resource-limited settings. Studies in which treatment was optimized based on results of resistance test found that the time to virological suppression was similar irrespective of baseline susceptibility.\(^{1,3,13,38-40,42,43}\) Resistance testing before initiation of ART is recommend in areas where the prevalence of transmitted resistance is unknown or greater than 5% (United States)\(^{44}\) or 10% (Europe).\(^{45}\) WHO has suggested that drug resistance testing should be considered prior to initiate ART when the prevalence of transmitted drug resistance is greater than 5%.\(^{46}\) The emergence of primary drug resistance with increasing prevalence in Thailand as mentioned above should be taken seriously and drug resistance testing should be considered before initiating ART in HIV-infected patients particularly those who are intravenous drug users or have partners taking ART with unreliable adherence. Clinicians should use the results of resistance test to select ART combinations that incorporate drugs to which the virus is fully susceptible and to investigate the resistance profile of the source. Optimal approach to make drug resistance testing accessible for Thai patients must be done, such as developing less expensive in-house resistance test and facilitating the processes of laboratory performance, result interpretation and reporting system. The national effort to improve treatment outcomes through rapid delivery of ART must be coordinated with the national evaluation of primary HIV drug resistance.

References


