

HIV-1 Drug Resistance among Antiretroviral-naïve HIV-1-infected Patients in Asia: Results from the TREAT Asia Studies to Evaluate Resistance- Monitoring Study (TASER-M)

Somnuek Sungkanuparph^{1*}, Rebecca Oyomopito², Suneer Sirivichayakul³, Thira Sirisanthana⁴, Patrick C K Li⁵, Pacharee Kantipong⁶, Christopher K C Lee⁷, Adeeba Kamarulzaman⁸, Matthew G Law⁹, Jeffery Smith⁹, Praphan Phanuphak²; on behalf of TASER-M

¹Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; ²National Centre in HIV Epidemiology and Clinical Research, UNSW, Sydney, Australia; ³HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand; ⁴Research Institute for Health Sciences, Chiang Mai, Thailand; ⁵Queen Elizabeth Hospital, Hong Kong, China; ⁶Chiang Rai Regional Hospital, Chiang Rai, Thailand; ⁷Hospital Sungai Buloh, Kuala Lumpur, Malaysia; ⁸University of Malaya, Kuala Lumpur, Malaysia; ⁹Formerly TREAT Asia, amfAR – The Foundation for AIDS Research, Bangkok, Thailand



BACKGROUND

Antiretroviral therapy (ART) has been scaled up in Asia for 2-9 years, depending on the countries and settings. Primary HIV drug resistance (HIV DR) threatens the effectiveness of ART among HIV-infected patients who are initiated ART. However, data of primary HIV DR in Asia is scanty. There are few widely available antiretroviral regimens in this region, especially in countries with limited resources, highlighting the importance of monitoring of HIV DR.

TREAT Asia (Therapeutics, Research, Education and AIDS Training in Asia) is a network of clinics, hospitals and research institutions working to ensure safe and effective delivery of HIV/AIDS treatments throughout Asia. To assess the extent of HIV DR in Asia, TREAT Asia has developed the TREAT Asia Studies to Evaluate Resistance-Monitoring Study (TASER-M). TASER-M objectives are to assess the prevalence and incidence of emerging HIV DR and to produce evidence to inform future treatment guidelines.

METHODS

The TASER-M protocol is harmonized with the WHO HIV DR monitoring survey methodology. Patients eligible for TASER-M are those initiating first-line or switching to second-line ARTs. Antiretroviral-naïve patients who were initiated on ART at participating sites during April 2007-March 2009 were studied. Patients who were exposed to PMTCT, monotherapy, or duotherapy were excluded from this analysis.

Genotypes were performed locally using externally quality-controlled in-house and commercial assays on samples collected within 6 months prior to initiating ART. HIV-1 drug resistance-associated mutations (RAMs) were assessed using IAS-USA 2008 criteria. Univariate and multivariate analysis were used to determine factors associated with HIV DR.

RESULTS

A total of 682 patients from 8 sites in Hong Kong (2), Malaysia (2), and Thailand (4) were studied. The mean (SD) age was 38.2 (10.1) years; 65.5% were male. Figure 1 shows the ethnicities of patients in this study. The majority (76.2%) of patients reported heterosexual contact as their primary risk exposure for HIV (Figure 2). The median (IQR) CD4 cell count and HIV-1 RNA were 100 (34-201) cells/mm³ and 100,000 (43,581-6,040,000) copies/mL, respectively. Overall, 77.7% had HIV-1 subtype CRF01_AE (Figure 3).

Figure 1. Ethnicities of 682 patients.

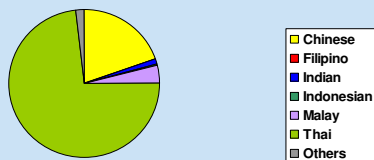


Figure 2. Primary risk exposures for HIV in 682 patients.

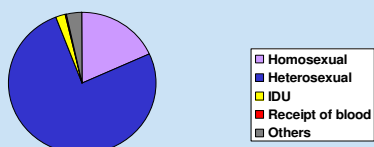
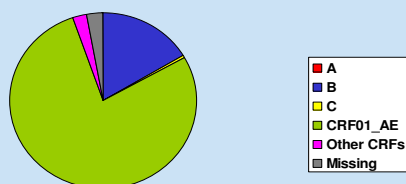


Figure 3. HIV-1 subtypes in 682 patients.



RESULTS

The prevalence of patients with ≥ 1 RAM(s) in any drug class was 13.8%. Patients had ≥ 1 NRTI-RAM (8.4%), ≥ 1 NNRTI-RAM (6.5%), and ≥ 1 PI-RAM (0.4%), as shown in Figure 4. K70R was the most common NRTI-RAM (7.6%); M41L, D67N, T69S, M184V, L210W, T215Y, and K219Q were observed $< 1\%$. For NNRTI-RAMs, efavirenz-RAMs and efavirenz/nevirapine (EFV/NVP)-RAMs were found in 6.5% and 0.6% of patients, respectively. Figure 5 demonstrates the distribution of RAMs observed in this study.

Figure 4. Prevalence of patients with ≥ 1 RAMs by drug classes

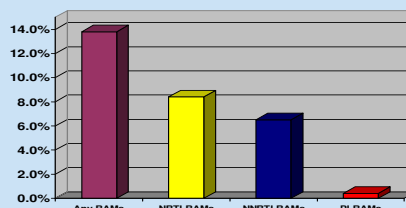
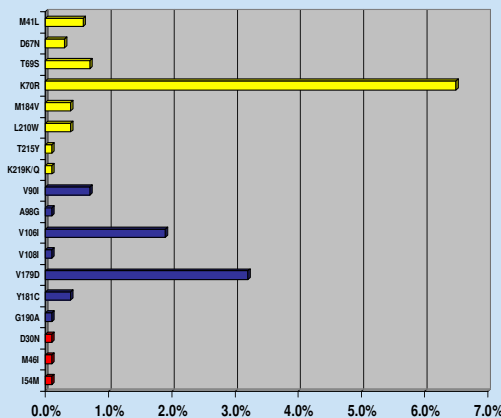


Figure 5. Prevalence of each RAM



Median CD4 cell count was significantly lower in patients with than those without RAMs (66 vs. 108 cells/mm³, $p=0.009$). There were no differences between those with and without RAMs in age, gender, site location, ethnicity, risk exposure, HIV-1 subtype, HBV co-infection, HCV co-infection, or HIV-1 RNA.

CONCLUSION

Primary HIV DR is emerging in Asia after more than 5 years of rapid ART scale-up. Patients with lower pre-ART CD4 cell count were at higher risk for having HIV DR. Although HIV genotype testing prior to ART initiation is not routinely recommended in resource-limited settings, our results raise concerns about the risk of early treatment failure in our cohort if genotype testing is not conducted.

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The TREAT Asia Studies to Evaluate Resistance
PCK Li⁵ and MP Lee, Queen Elizabeth Hospital and KH Wong, Integrated Treatment Centre, Hong Kong, China;
N Kumarasamy⁸ and S Saghayam, YRG Centre for AIDS Research and Education, Chennai, India;
S Pujari³ and K Joshi, Institute of Infectious Diseases, Pune, India;
TP Herati⁴ and F Yuliana, Faculty of Medicine, Udayana University & Sanglah Hospital, Bali, Indonesia;
CKC Lee⁷ and LL Low, Hospital Sungai Buloh, Kuala Lumpur, Malaysia;
A Kamarulzaman⁸ and LY Ong, University of Malaya, Kuala Lumpur, Malaysia;
R Dhangaraj and R Capistrano, Research Institute for Tropical Medicine, Manila, Philippines;
YMA Chen⁵, WW Wong and YW Yang, Taipei Veterans General Hospital and AIDS Prevention and Research Centre, National Yang-Ming University, Taipei, Taiwan;
P Phanuphak² and S Sirivichayakul, HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand;
S Sungkanuparph¹ and B Piyaong, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;
T Sirisanthana⁴ and J Praparattanapan, Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand;
P Kantipong⁶ and P Kambua, Chiang Rai Regional Hospital, Chiang Rai, Thailand;
AH Sohn, L Messerschmidt⁹ and T Singtoro, TREAT Asia, amfAR – The Foundation for AIDS Research, Bangkok, Thailand;
DA Cooper, MG Law⁹ and R Oyomopito, National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney, Australia.

† Steering Committee Chair, ‡ Steering Committee Co-Chair, * Steering Committee member
§ Protocol Chair, ¶ Protocol Co-Chair

