

# Why Should We Have Tenofovir in Thailand?

Somnuek Sungkanuparph, M.D.<sup>1,2</sup>

William G Powderly, M.D.<sup>2</sup>

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Highly active antiretroviral therapy (HAART) has dramatically reduced the morbidity and mortality in HIV-infected patients. Currently, almost all US FDA-approved antiretroviral drugs are available in Thailand, except for tenofovir disoproxil fumarate, emtricitabine (FTC), delavirdine (DLD), amprenavir (APV), and enfuvirtide (T-20). Among these, FTC, DLD, and APV can be equally substituted with other antiretroviral drugs available in Thailand; T-20 is very expensive and reserved for highly experienced HIV-infected patients; but this is not the case for tenofovir. Considering the current situation of antiretroviral therapy in Thailand, we need to have TDF available as an option. Why?

In 2004, there are estimated to be 600,000 living HIV-infected patients in Thailand.<sup>1</sup> About 5,000 Thais now receive GPO-VIR, a generic combined pill of d4T/3TC/nevirapine (NVP). By the time Thailand hosts the XV International AIDS Conference in July 2004, the ministry of public health plans to offer GPO-VIR to 60,000 HIV-infected patients in the country.<sup>2</sup> However, the long-term efficacy of the regimen will be limited by long-term complications and by emerging viral resistance. We can anticipate the “synchronizing” viral resistance patterns in the majority of Thai HIV-infected patients in the future when these people fail GPO-VIR. From previous studies,<sup>3-8</sup> we can predict the emergence of M184V, thymidine analogue mutations (TAMs),

K103N, and Y181C mutations in reverse transcriptase (RT) gene. This mutational pattern greatly limits options among other RT inhibitors. The next best HAART regimen for HIV-infected patients who fail GPO-VIR with these mutations would be a regimen of a (boosted) protease inhibitor with didanosine (ddI) and tenofovir.<sup>9-12</sup> In the absence of tenofovir, a potent second-line HAART regimen for these patients is nearly not possible. This is the main reason why we need to have tenofovir in Thailand. In addition, the availability of tenofovir will also make the once daily HAART regimen, an option for initial treatment, possible in Thailand. Evidence from various studies show that once daily regimen can improve adherence to antiretroviral therapy and lead to the better outcome.<sup>13,14</sup>

The fact that the background prevalence of hepatitis B virus (HBV) infection in Thai population is high,<sup>15,16</sup> raises a second important reason for the availability of tenofovir in Thailand. Previous studies of HBV/HIV co-infection in Thailand shows the prevalence of 9 percent in HIV-infected population.<sup>17</sup> HIV infection alters the natural history of HBV infection, leading to more severe liver disease, decreased hepatitis B e antigen seroconversion, and higher HBV DNA levels.<sup>18-20</sup> Tenofovir is a very promising drug for the treatment of chronic hepatitis B in HIV-infected individuals. Previous studies demonstrate that tenofovir

<sup>1</sup>Infectious Diseases Unit, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

<sup>2</sup>Washington University School of Medicine, St Louis, MO, United States.

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Reprint request: Somnuek Sungkanuparph, M.D., Infectious Diseases Unit, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

has potent anti-HBV efficacy in antiretroviral therapy-experienced and -naïve individuals co-infected with HIV and HBV.<sup>21,22</sup> Tenofovir is also active against 3TC-resistant HBV variants in HBV/HIV co-infected and HBV mono-infected patients.<sup>22-26</sup> The availability of tenofovir in Thailand will improve the treatment outcome of chronic hepatitis B in both HBV mono-infected and HBV/HIV co-infected patients in the country.

Given there are important reasons as mentioned above, why don't we have tenofovir in Thailand? Currently, there is no branch of Gilead, the pharmaceutical company that manufactures tenofovir (Viread), in Thailand. A widely used product of Gilead, AmBisome (liposomal amphotericin B), is currently distributed in Thailand by a local drug company, Siam Pharmaceuticals. Both companies have not decided to launch tenofovir in Thailand, even though tenofovir has been approved by US FDA and widely used in the United States since 2001. The drug companies are mainly targeting this drug in naïve HIV-infected patients. In April 2002, the Government Pharmaceutical Organization had produced GPO-VIR. This much cheaper combined pill might have influenced the decision of both Gilead and Siam Pharmaceuticals to launch tenofovir in Thailand. However, we believe that there is a substantial market for tenofovir in Thailand, notwithstanding an ethical issue in provision of potentially-health preserving medication. This drug will be definitely needed in Thailand in the near future. Without potent second-line drug regimens for our (thousands of) HIV-infected patients who fail GPO-VIR, the epidemiology of HIV/AIDS in Thailand will be a different story. To accomplish the goal of having tenofovir in Thailand, HIV/AIDS experts in Thailand need to address this concern to the ministry of public health, Gilead and Siam Pharmaceuticals, and academic institutes in the country. In the mean time, while the availability of tenofovir is not reliable in Thailand, appropriate use of GPO-VIR to eliminate the emerging viral resistance (i.e. strict adherence, avoid in previous

mono- or duo-therapy) is strongly recommended. Strong and consistent HIV prevention interventions in the country are necessary to control transmission of resistant HIV. Otherwise, we will not even have promising initial HAART regimens for resistant-HIV-infected patients.

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