CHAPTER VI

CONCLUSION

In the present study, the prevalence of AZT-resistant 215 mutant was investigated in HIV-1 infected Thai patients in which majority carries HIV-1 subtype E. To amplify and detect codon 215 of HIV-1 RT gene of both subtype B and E, the previously described selective PCR needs to be modified. Interesting, the outer "sense" primer (L1M) failed to amplified HIV-1 subtype E but not in the case of subtype B. It suggestes that there is a genetic variation occurred at position 2554-2556 of RT gene among the two subtypes.

There was no evidence of transmission of AZT-resistant mutant in the AZT-naive Thai subjects, whereas a current report of HIV-1 infected patients with no prior AZT treatment in Spain carried AZT-resistant mutant up to 30%.[119] Twenty two percents (11 of 50) and 42% (21 of 50) of the patients who had been treated with AZT for less than 6 months (group II), and for more than 6 months (group III), respectively, were showed AZT-resistant genotype. In the group II, the means CD4 cell counts of the patients who carried codon 215 mutant were significantly lower than that of the ones who carried wild type virus (63.6 $\pm$ 50.2 vs. 132.5 $\pm$ 107.6 in the group II, $p < 0.05$).

In the prospective study, 7 of the 10 patients (70%) develpoed AZT-resistant genotype between 6 to 12 months of AZT monotherapy.

In summary, the nature of AZT-resistance of HIV-1 subtype E is similar to the previously reported in subtype B, which is monotherapy with AZT could induce resistant mutant in a more rapid fashion in more advanced patients. These findings also emphasize that monotherapy should be no longer considered as a treatment of choice of HIV infection. Thus, this is strongly supported the Thai National Guidelines

for clinical use of Antiretroviral Agents has recently implied the strategy of "hit early and hit hard with combination therapy",[120-122] by the recommendation of initiating combination treatment with either AZT+ddI or AZT+ddC in patients who have CD4+ cell counts below 350 cells/μL.