Editorial

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Regional Experience of Abacavir: Valuable but Still has Unanswered Question

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Abacavir (ABC) is one of the most widely recommended nucleoside reverse transcriptase inhibitors (NRTIs) and is relatively safe for patients with renal insufficiency or decreased bone mineral density [1, 2]. Furthermore, besides being a single-component tablet (Ziagen®), ABC is also marketed as a fixed-dose combination tablet with lamivudine (Kivexa® or Epizicom®) and lamivudine + dolutegravir (Triumeq®), which improves patients' convenience and compliance. However, like most antiretroviral agents, ABC was introduced in Korea without any regional preapproval clinical data. Thus, clinicians in Korea should begin to prescribe most antiretroviral agents, including ABC, without any local experience. Considering that the efficacy and frequency of adverse events of drugs would be variable in different ethnic groups, these conditions are somewhat dissatisfying from the standpoint of clinicians.

In the current issue of *Infection & Chemotherapy*, Ann et al. reported post-marketing experiences with ABC [3]. A total of 669 patients were enrolled, and 1,047.8 person-years were observed. Considering that post-marketing data are only tools to assess the safety and efficacy of antiretroviral agents at the regional level, the study must be valuable for clinicians in Korea.

The most important concern in using ABC is the fatal hypersensitivity reaction associated with HLA-B*5701 [4]. Ann et al. reported only one possible hypersensitivity reaction in which case results of HLA-B*5701 and confirmatory patch tests were not available [3]. Considering that only one case of ABC hypersensitivity reaction was possible among the 669 patients, we could say that ABC hypersensitivity is rare in Korean patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). Thus, we could say that careful monitoring for ABC hypersensitivity reaction without HLA-B*5701 is a practical clinical option in Korea.

Although inconclusive, cardiovascular adverse events have been another important concern when prescribing ABC [5-7]. In their study, Ann et al. reported no case of ischemic heart disease [3]. However, I think these results should be interpreted with caution. The relationship between ABC use and cardiovascular adverse events has been issued since 2008. Thus, we could say that clinicians might avoid prescribing ABC to patients with higher cardiovascular risk factors since 2008. The current study of Ann et al. was conducted from June 2010 to Jun 2016, which is the period after the possibility of ABC-related cardiovascular adverse events became controversial. In

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my opinion, avoiding ABC in patients with higher cardiovascular risk might result in no or few cardiovascular events. To clarify this issue, the authors should represent the cardiovascular risk scores (*e.g.*, the Framingham risk score) of the subjects. However, as usual in a post-marketing study, the authors did not do so. The authors mentioned Japanese studies that reported no ABC-related cardiovascular events [8, 9]. In these Japanese studies, most subjects were enrolled before 2008. Considering the results of the current study of Ann et al. and the two Japanese studies, we can say that no evidence exists for the relationship between ABC use and cardiovascular diseases in the East Asian ethnic group, but some underestimation may be possible.

In the current study by Ann et al., 315 adverse events were reported in 1,047.8 person-years of observation, with 4 cases of more severe adverse events. As the authors mentioned, the incidence of adverse events in the current study was relatively lower than that of a Japanese study [8]. In this context, we could say that ABC is well tolerated in Korean patients with HIV/AIDS.

The effectiveness of ABC in the current study of Ann et al. was satisfactory. Of 76 patients with results of peripheral blood HIV-1 RNA levels at 24 months available, 90.8% achieved viral suppression. In addition, the mean CD4+ T-cell count increased by 242.9 cells/mm^3 (334.7 cells/mm^3 → 577.6 cells/mm^3) after 24 months of ABC use. As the authors reported, as this study has no comparative arm, we cannot evaluate the exact efficacy of ABC. However, we can say that ABS is effective for most patients with Korean HIV/AIDS.

Despite some limitations as usual in post-marketing studies, this study might have important messages to clinicians. First, ABC is generally safe and effective for Korean patients with HIV/AIDS. Second, ABC hypersensitivity is rare in Korean patients with HIV/AIDS. However, the risk of cardiovascular adverse events is still inconclusive.

Conflicts of Interest

No conflicts of interest.

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References

1. AIDS info. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. Accessed 12 September, 2017.
2. Korean Society for AIDS. The 2015 clinical guidelines for the diagnosis and treatment of HIV/AIDS in HIV-infected Koreans. Infect Chemother 2015;47:205-11.
3. Ann H, Kim KH, Choi HY, Chang HH, Han SH, Kim KH, Lee JS, Kim YS, Park KH, Kim YK, Sohn JW, Yun NR, Lee CS, Choi YW, Lee YS, Kim SW. Safety and efficacy of Ziagen (abacavir sulfate) in HIV-infected Korean patients. Infect Chemother 2017;49:205-12.
4. Mallal S, Phillips E, Carosi G, Molina JM, Workman C, Tomazic J, Jägel-Guedes E, Rugina S, Kozyrev O, Cid JF, Hay P, Nolan D, Hughes S, Hughes A, Ryan S, Fitch N, Thorborn D, Benbow A; PREDICT-1 Study Team. HLA-B*5701 screening for hypersensitivity to abacavir. N Engl J Med 2008;358:568-79.
5. D:A:D Study Group, Sabin CA, Worm SW, Weber R, Reiss P, El-Sadr W, Dabis F, De Wit S, Law M, D'Arminio Monforte A, Friis-Møller N, Kirk O, Pradier C, Weller I, Phillips AN, Lundgren JD. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. Lancet 2008;371:1417-26.
6. Worm SW, Sabin C, Weber R, Reiss P, El-Sadr W, Dabis F, De Wit S, Law M, Monforte AD, Friis-Møller N, Kirk O, Fontas E, Weller I, Phillips A, Lundgren J. Risk of myocardial infarction in patients with HIV infection exposed to specific individual antiretroviral drugs from the 3 major drug classes: the data collection on adverse events of anti-HIV drugs (D:A:D) study. J Infect Dis 2010;201:318-30.
7. Ding X, Andraca-Carrera E, Cooper C, Miele P, Kornegay C, Soukup M, Marcus KA. No association of abacavir use with myocardial infarction: findings of an FDA meta-analysis. J Acquir Immune Defic Syndr 2012;61:441-7.
8. Kurita T, Kitaichi T, Nagao T, Miura T, Kitazono Y. Safety analysis of Ziagen® (abacavir sulfate) in postmarketing surveillance in Japan. Pharmacoepidemiol Drug Saf 2014;23:361-71.
9. Kurita T, Kitaichi T, Nagao T, Miura T, Kitazono Y. Safety analysis of Epzicom® (lamivudine/abacavir sulfate) in post-marketing surveillance in Japan. Pharmacoepidemiol Drug Saf 2014;23:372-81.