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Lamivudine/Zidovudine/Abacavir

A Viewpoint by Graeme Moyle

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Triple nucleoside analogue therapy with the lamivudine, zidovudine plus abacavir triple combination tablet (Trizivir™) provides simple food-independent twice-daily therapy for patients with HIV infection. However, studies of initial therapy suggest that the efficacy of this regimen may be suboptimal when initiated in persons with a baseline HIV RNA levels greater than 100 000 copies/mL.[1] Several switch studies have reported data indicating that switching from initial successful therapy to the combination of lamivudine, zidovudine plus abacavir maintains virological efficacy[2,3] and may improve metabolic parameters.[4] Data on this triple nucleoside analogue combination in persons who initiated their original HAART with viral loads >100 000 copies/mL and then switched indicate that lamivudine/zidovudine/abacavir 'maintenance' therapy after an initial 'induction' antiretroviral therapy regimen maintains virological control regardless of high viral load (>100 000 copies/mL) and low CD4+ cell count (<100 cells/μL) prior to the initiation of antiretroviral therapy.[5] However, evidence from the Swiss maintenance therapy study indicated that individuals who have archived nucleoside analog mutations through prior treatment failure or use of thymidine analog-based dual or monotherapy regimens are at increased risk of losing virological control if successful protease inhibitor-based triple therapy is substituted for lamivudine, zidovudine plus abacavir.[3]

The use of the lamivudine/zidovudine/abacavir triple combination tablet would therefore appear to be optimal as a substitution or simplification treatment for persons who are on a first-line therapy or who have not failed treatment and are therefore unlikely to be harboring nucleoside analogue mutations. The data suggest several potential approaches for the use of the triple combination tablet this way. Firstly, in patients receiving an initial treatment regimen that they wish to simplify in terms of reducing tablet number and dosing complexity, or who have metabolic disturbances such as elevated lipids or evidence of insulin resistance; such individuals could directly substitute their treatment with the triple combination tablet. Additionally, women on a first-line therapy with an efavirenz-based regimen who wish to consider pregnancy in the future may consider the triple combination tablet as an appropriate combination to change to before pregnancy. The second approach for use of this triple combination tablet would be as initial therapy with the inclusion of a fourth agent until a full virological control was achieved, thereafter withdrawing the fourth agent, leaving the patient on the lamivudine/zidovudine/abacavir triple combination tablet alone. This approach is currently being investigated using efavirenz as the fourth agent and evaluating the suitability of efavirenz withdrawal at several timepoints after treatment initiation. Other fourth agents that may be considered in this approach would include tenofovir, didanosine or nevirapine. ▲

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