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Emtricitabine

A Viewpoint by Erik De Clercq

Rega Institute for Medical Research, Katholieke Universiteit, Leuven, Belgium

Emtricitabine (Emtriva™) has been recently approved by the US FDA for use in combination with other antiretroviral agents for the treatment of HIV infection. Following zidovudine (AZT), didanosine (ddI), zalcitabine (ddC), stavudine (d4T), lamivudine (3TC) and abacavir (ABC), emtricitabine (also known as (−)FTC) is the seventh nucleoside reverse transcriptase inhibitor (NRTI) to be approved for the treatment of HIV. Other recently approved anti-HIV drugs include the nucleotide reverse transcriptase inhibitor (NtRTI) tenofovir disoproxil fumarate, the protease inhibitor atazanavir and the virus-cell entry inhibitor enfuvirtide.

Unlike AZT, ddI, ddC, d4T and ABC, but like 3TC, emtricitabine is an L-nucleoside analogue. Although structurally and mechanistically similar to 3TC, emtricitabine appears to be more potent in terms of anti-HIV activity. This is also reflected by a more efficient inhibition of HIV-1 reverse transcriptase (RT) by (−)FTC 5′-triphosphate as compared to 3TC 5′-triphosphate. In addition, the RT resistance mutation (M184V) that emerges following the use of 3TC is also seen with (−)FTC but, seemingly, at a lower frequency.

The efficacy of emtricitabine, as part of triple-drug therapy, has been demonstrated in both adults and children. In one particular study that enrolled 571 treatment-naive patients who were randomised to receive once-daily emtricitabine or twice-daily stavudine, in combination with didanosine and efavirenz, emtricitabine proved clearly superior to stavudine: at week 60, 79% of the patients receiving emtricitabine (n = 286) had a persistent suppression of HIV RNA <400 copies/mL, as compared to 63% of the patients receiving stavudine (n = 285). Also tolerability in the emtricitabine arm was better than in the stavudine arm. The most common adverse events occurring in patients receiving emtricitabine were headache, diarrhea, nausea and rash, and all were generally mild to moderate in severity.

Emtricitabine is conveniently used at a single daily pill (capsule) of 200mg. This once-daily dosing has become a new strategy in the therapy of HIV infections as nowadays other anti-HIV drugs such as atazanavir (400mg), efavirenz (600mg) and tenofovir disoproxil fumarate (300mg) are also administered on a once-daily basis. It may even be feasible to combine some of these different anti-HIV drugs into one pill, and this co-formulation is currently envisaged for the combination of emtricitabine and tenofovir. If further combined with efavirenz, this triple-drug therapy may well be one of the most efficacious anti-HIV drug cocktails that have ever been concocted. ▲