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Emtricitabine/Tenofovir Disoproxil Fumarate

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One of the keys to antiretroviral therapy success is good adherence. In fact, it has to be more than that: *good enough* means taking 90–95% of the entire regimen. To help patients achieve this, there has been a move towards once-daily therapy. Several drugs have been developed for once-daily use and some agents that are usually administered twice daily (e.g. saquinavir or abacavir) can be given as part of once-daily treatment regimens. Simplifying therapy to further improve adherence might be achieved by combining two or more compounds into one pill. However, such combinations are few and far between. Currently only zidovudine/lamivudine and lopinavir/ritonavir have been licensed, but for twice-daily use, and an abacavir/lamivudine combination will soon be available. Emtricitabine/tenofovir disoproxil fumarate (tenofovir DF) is a novel co-formulation with many advantages. The pill burden will be only one tablet a day, meaning that a highly active antiretroviral therapy (HAART) regimen can be constructed with only two pills once daily. In fact, it has been announced that the co-formulation of emtricitabine and tenofovir DF will be combined with the nonnucleoside efavirenz, giving a single-pill HAART regimen.

The combination of emtricitabine and tenofovir DF has other advantages. Toxicity is low, there is no major issue with food requirements and it can generally be combined with non-nucleosides and boosted proteases without any important drug interactions. One exception is that tenofovir DF and atazanavir may interact, resulting in lower atazanavir levels. This is overcome by boosting atazanavir with low-dose ritonavir. Both tenofovir DF and emtricitabine are effective against hepatitis B, which is an added advantage for patients co-infected with HIV and hepatitis B. These patients can have both their viral illnesses treated with similar drug regimens, with little risk of inducing hepatitis B resistance associated with the tyrosine-methionine-aspartate-aspartate motif.

The efficacy of emtricitabine and tenofovir DF in combination with efavirenz will become clear when the Gilead 834 study is completed. In the meantime, In the meantime, two recently published papers showed the efficacy and tolerability of the individual compounds tenofovir DF (with lamivudine)[1] and emtricitabine (with didanosine)[2] when combined with efavirenz in antiretroviral-naive patients. Extremely high rates of viral suppression and low rates of toxicity occurred with these regimens and it would be difficult to contemplate a much different result when the two agents are given as the backbone to efavirenz. The administration of co-formulated emtricitabine/tenofovir DF may be preferred over coadministration of lamivudine and tenofovir, since the latter must be given as separate agents. Whether there will be less resistance with the co-formulated tablet (because it will not be possible to take the two agents separately) needs to be explored.

Finally, the issues of cost and availability still have to be resolved. These face all providers of healthcare, especially in developing countries. ▲

References

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